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Table of Contents

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ORIGINAL ARTICLES— Page

The Surgery of Atrial Defects with Special Reference to the Septum Primum, by Rowan Nicks and A. F. Grant .. 201
Study in the Efficiency of Vaccination against Influenza in Two Employment Groups in Melbourne in 1959, by A. E. Duxbury and T. E. B. Keen .. 206
Trimeprazine ("Vallergan"): Its Assessment as an Antipruritic, by Eric H. Taft, Brian R. Entwisle, and Russell Langley .. 208
The Use of a Papain Solution of Approximately pH 3·0 in Rh Testing and Atypical Antibody Detection, by J. A. Albrey and R. T. Simmons 210
Trial of "Orasecron" as a Pregnancy Test, by W. J. Rawlings .. 213
An Apparatus to Aid in the Treatment of the Fractured Radial and Ulnar Shafts, by D. D'A. Webling .. 214

REPORTS OF CASES—

A Case of Idiopathic Hypoparathyroidism Presenting as Idiopathic Epilepsy, by Ian G. Lyall 215
Severe Respiratory Infection Presenting with Coma, by Clement R. Boughton and Eleanor M. Robinson .. 218
Acquired Agammaglobulinæmia, by J. Hansky .. 220

REVIEWS—

Diagnosis and Treatment of Menstrual Disorders and Sterility .. 221
Arterial Embolism in the Limbs .. 222
Systemic Lupus Erythematosus .. 222
Cholera .. 222
Recent Studies in Epidemiology .. 222
Womanhood .. 223
An Atlas of Normal Radiographic Anatomy .. 223
Text-book of British Surgery .. 223
Progress in Radiation Therapy .. 223
Proceedings of a Symposium on Immunization in Childhood .. 223
Fundamental Techniques of Plastic Surgery and their Surgical Applications .. 224
Radiation Biology of Vicia Faba in Relation to the General Problem .. 224

BOOKS RECEIVED .. 224

LEADING ARTICLES—

The Control of Tuberculosis in Australia .. 225
A Munificent Gift for Rheumatism Research .. 225

CURRENT COMMENT— Page

The Incidence of Sheehan's Syndrome .. 226
Dental Caries and Soil Constituents in New Zealand 227
Marsupial Milk .. 227

ABSTRACTS FROM MEDICAL LITERATURE—

Orthopædic Surgery .. 228
Pædiatrics .. 229

BRUSH UP YOUR MEDICINE—

Essential Hypertension .. 230

OUT OF THE PAST .. 231

MEDICAL MATTERS IN PARLIAMENT—

House of Representatives .. 232
Senate .. 233

CORRESPONDENCE—

The Organization of the Profession .. 234
Trachoma in Western Australia .. 234
Surgery and the General Practitioner and Professional Unity .. 235
International Association for Dental Research: Australian Section .. 235
Total Blindness from Temporal Arteritis .. 235
Attempted Suicide, with Special Reference to Bromureides and Similar Preparations .. 236
Smallpox Vaccination .. 236

POST-GRADUATE WORK—

The Post-Graduate Committee in Medicine in the University of Sydney .. 236
Third Australasian Conference on Radiobiology .. 236
Royal Prince Alfred Hospital: Ear, Nose and Throat Department .. 237
The Melbourne Medical Post-Graduate Committee 237

NOTES AND NEWS .. 238

NOTICE—

British Medical Association: Victorian Branch .. 239

NAVAL, MILITARY AND AIR FORCE—

Appointments .. 239

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA .. 239

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—

New South Wales .. 240

NOMINATIONS AND ELECTIONS .. 240

DEATHS .. 240

DIARY FOR THE MONTH .. 240

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 240

EDITORIAL NOTICES .. 240

THE SURGERY OF ATRIAL DEFECTS WITH SPECIAL REFERENCE TO THE SEPTUM PRIMUM.[1]

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THE surgical experience of the Royal Prince Alfred Hospital with atrial septal defects is presented in the hope that it may provide some basis for discussion of the problems encountered during our development phase of intracardiac surgery. A number of complicated conditions, including anomalous pulmonary veins and septum primum defects, have been encountered and treated. This material is summarized in Figure I.

Definitions.

The secundum defect is a superior opening in the septum, either at the foramen ovale or in the membraneous atrial septum (Figure I, Sections 1, 2, 3, 4 and 5).

The ostium primum defect is defined as an opening low down in the atrial septum just above normal mitral and tricuspid atrio-ventricular valves. The lower rim of the defect is formed by the annulus of the atrio-ventricular valves, and the upper rim by the well-defined lower border of the atrial septum (Figure I, Section 6).

The atrio-ventricularis communis defect includes any atrial defect in which there is maldevelopment of the endocardial cushions. The contiguous septal leaflets of the mitral or tricuspid valves are cleft to varying degrees. In partial atrio-ventricularis communis defects only one valve (usually the mitral) is cleft and the ventricular septum closed. Complete atrio-ventricular defects are characterized by clefts both in the anterior leaflet of the mitral valve and in the septal leaflet of the tricuspid valve. There is frequently a ventricular septal defect as well (Figure I, Sections 7 and 8).

Embryology of Atrial Septal Defects.

By the sixth week of intrauterine life the division of the heart into chambers and right and left sides is apparent. On the outside there are constrictions demarcating the atrial and ventricular chambers, and on the inside there are ridges which will form the septa dividing the chambers into right and left sides, and also endocardial cushions interposed between the atrial and ventricular ridges which will complete the division and form the valves.

[1] Read at a meeting of the Cardiac Society of Australia and New Zealand.

As the common venous entrance of the sinus venosus becomes moved to the right side, the prominent dorsal and cephalically situated atrial ridge (septum primum) appears on its left side and grows, until by fusion with the dorsal and the ventral endocardial cushions (which in turn are already fused with the ventricular septum) it closes the communication with the left side of the heart below.

As this happens, the septum breaks down above, to keep open a by-pass into the left atrium through the foramen ovale. A further ridge, the limbus, appears on the right side of the septum primum. The ends of this ridge grow down and fuse with the atrio-ventricular endocardial cushions to form a peripherally situated thickening all round. This is incorporated into the septum primum except at its free posterior margin, which persists and overlaps the foramen ovale as a valve. This valve serves to divert blood to the left atrium in utero, but prevents reversal after birth.

Superior septal defects occur with inadequate differential growth of the secundal ridge, deficiencies in the septum primum and abnormal venous drainage.

The cardiac muscle underlying the atrio-ventricular constriction is replaced by fibrous valve rings except for a bundle of embryonic muscle fibres posteriorly. This bundle grows down from the atrio-ventricular node (situated below and in front of the coronary sinus) through the atrio-ventricular ring to bifurcate at the top of the muscular ventricular septum into right and left branches. These branches are distributed subendocardially to the right and left ventricles respectively as the conduction bundle of His.

If development is arrested at the sixth week, there is complete failure of fusion of the endocardial cushions. This is manifest in the persistence of an inferior atrial septal defect together with a ventricular septal defect and a split in each of the mitral and tricuspid valve leaflets where they take origin from the septum. This is the atrio-ventricularis communis defect in its extreme form (Figure I, Section 8).

Lesser degrees of malfusion result in less serious malformations.

If the ventricular septum is closed, but one of the valvular elements to the septum remains unfused (usually mitral), the clinical lesion is a partial atrio-ventricularis communis defect. If the valve elements are perfectly formed, but a solitary inferior defect in the septum persists, this is the septum primum defect.

Pathological Observations.

A brief study of post-mortem records of the Royal Alexandra Hospital for Children, Sydney, during the period 1947-1958 revealed that 213 patients died from congenital heart disease. There were superior atrial defects in 26 (12%) and inferior atrial septal defects in 23 (11%). The majority of the inferior defects were of the atrio-ventricularis communis variety.

Pathological Anatomy of the Atrio-Ventricularis Communis Defect.

In most cases of severe malformation there is failure to thrive, and death occurs within the first year of life (vide Table I).

There are a left-to-right shunt at atrial level, regurgitation into the atria because of the deformed and split mitral and/or tricuspid valve leaflets, and a left-to-right shunt at ventricular level as well (if the lesion is complete). In severe forms with a ventricular defect, blood is pumped under the closed common valves into the aorta and pulmonary artery during ventricular systole, the relative flow varying with the size of the defect and the pulmonary vascular resistance.

In the most severe form, there is no closure at all of the large ventricular septal defect. There is no atrio-ventricular ring above the septum for the completely split valves to take seating, and the aortic ring takes common origin with the atrial valve. There is not tissue to suture or to patch. At present these deficiencies are deemed inoperable. In lesser degrees of the abnormality, in which the base of the aorta is sealed and the ventricular septal defect partially closed, the condition is not hopeless, provided the valves themselves are not grossly deformed.

There are three important anatomical considerations to be observed in attempting surgical repair: (i) the approximation of the valve rings to the top of the septum, with or without a patch, to provide a proper seating for the flimsy valve cusps; (ii) careful suture of the cleft mitral and tricuspid valves; (iii) closure of the atrial septal defect in such a way that the valves are not deformed, the suture line is not under tension and the conduction bundle is undamaged.

During life there is considerable and continual strain in the region of the valve ring from muscular activity. The repair must not be under tension. It is usually necessary to make up for the tissue deficiency by closing the defect with a plastic patch. Injury to the bundle of His at operation is best avoided by inserting the repair sutures to the left side of the defect anteriorly, where there is usually a fibrous rim. The left branch is safer, being broad and flat, while the right, being a narrow ribbon, is easily interrupted. The bundle of His passes forwards on the right of the inferior interatrial septum from the atrio-ventricular node (situated below and in front of the coronary sinus), and subendocardially through the fibrous skeletal ring to the top of the ventricular septum near the valve attachment to the defect, and immediately divides at the top of the muscular ventricular septum into right and left branches, which ramify beneath the endocardium of both ventricles.

Operation Techniques.

The techniques of operation are planned in accordance with the pre-operative diagnosis. Hypothermia is employed for predictably short procedures, and the cardio-pulmonary by-pass for more serious cases or for those which require a longer time for delicate suture.

Hypothermia Technique for Secundum Defects.

With good teamwork, straightforward defects of the secundum type are as a routine repaired under hypothermia within a time limit of eight minutes. As a high proportion of patients develop atrial fibrillation during manipulations under cooling, all are digitalized before operation.

After being cooled to 33·5° C. in a bath of iced water under anæsthesia, the patient is transferred to the operating table for surgery, and during this period the temperature drifts down to 31° C. over the next 30 minutes. After surgery, normal temperature is restored in a bath of warm water. In each phase the time taken in the bath is about 15 to 20 minutes. Mechanical ventilation is maintained during the whole period of unconsciousness.

Heparinized and artificially oxygenated blood is delivered into the coronary arteries during the period of venous occlusion by perfusion into the proximal end of the clamped aorta at a rate of 40 to 60 ml. per minute. This maintains the heart muscle in such a good state that the blood pressure is usually immediately restored on release of the caval tapes. It usually rises above normal to 160-180 mm. of mercury within seconds and gradually falls to the normal pre-operative level.

By the use of this technique, the defect is defined and lifted forwards with sutures at either end, and the septum is closed by running sutures, reinforced at intervals with single stitches.

Most pulmonary venous anomalies have been restored by diverting the abnormal venous orifice into the left atrium. If the pulmonary veins drain into the superior vena cava, this is partitioned in such a way that the superior vena caval blood, in front, drains into the right atrium, and pulmonary venous blood, behind, drains into the left atrium.

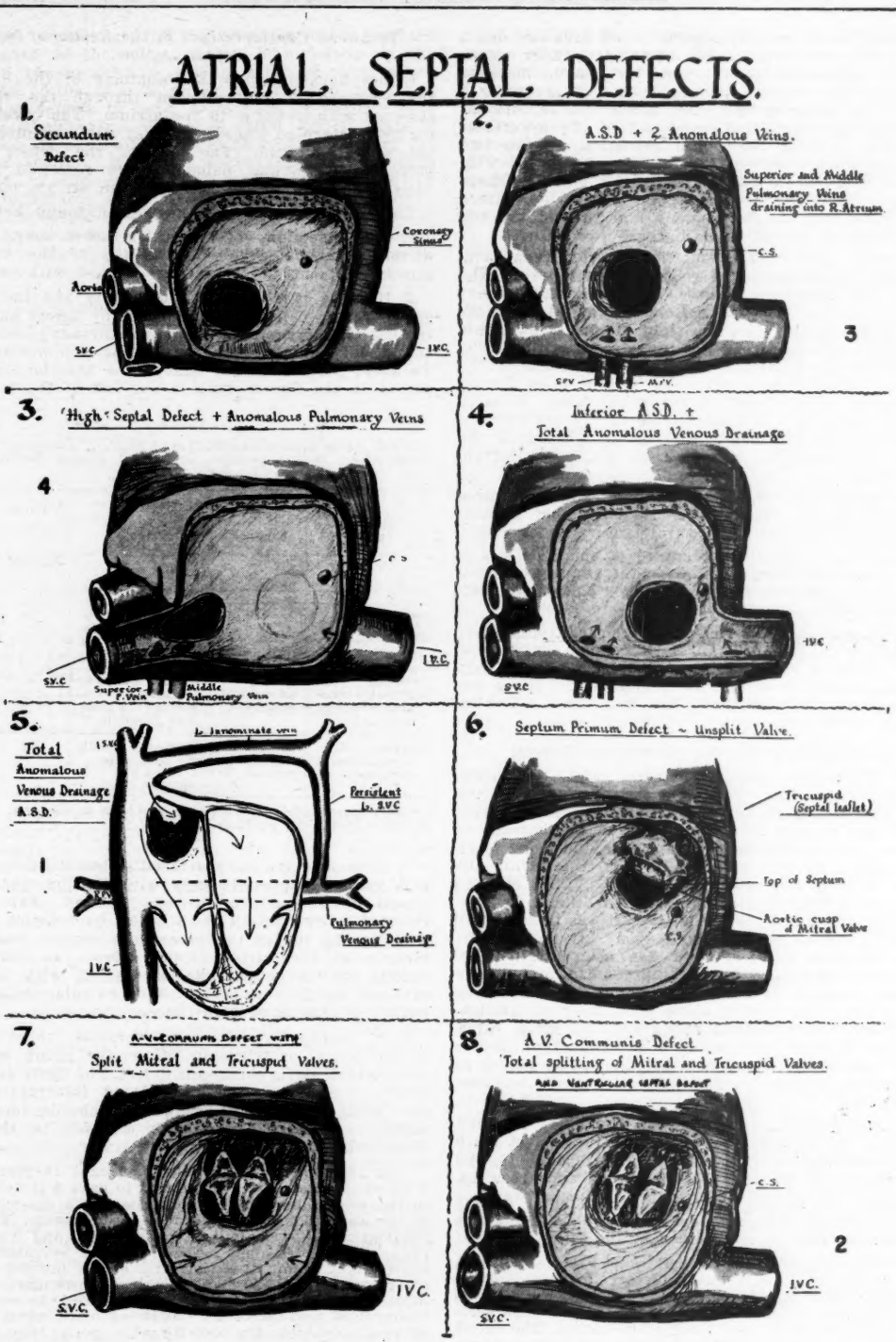

FIGURE I.

Diagrammatic representation of the surgical experience reported in this paper. The small letters represent the number of patients operated upon. Sections 1 to 5 illustrate superior septal defects in various situations. There were anomalous pulmonary veins draining into the right atrium in some cases, and these are shown in Sections 2, 3, 4 and 5. Sections 6, 7 and 8 depict inferior septal defects. The lower rim is the top of the interventricular septum. The valve attached to the septum may be unsplit (septum primum, Section 6) or split (atrio-ventricularis communis defect, Sections 7 and 8).

If the veins open into the superior vena cava low down near the defect, the division can be effected under vision by sutures approximating the anterior venous margins to the top of the defect. The upper end of the vein is sutured to the anterior reflection from the septum on to the vena cava, and the lower end of the lowermost vein to the back of the septal reflection. These two mattress sutures are placed from within by a thread with a needle at each end of the suture and tied outside. These demarcate the ends and a ridge for suture. A suture along between the anterior venous margin and the top of the septum is placed between these two sutures.

If the veins open high up on the superior vena cava, partitioning is accomplished without interrupting the circulation by inserting sutures around a "Polythene" tube placed in the vena cava from the atrial appendix and having an opening into the right atrium below. This allows venous return during the period of partition. The lower part of the partition is sutured as before to the top of the septal defect, with the atrium open during a short period of occlusion of the great veins. Heparin (3 mg. per kilogram) is administered to prevent clotting in the by-pass, and is neutralized on completion of the procedure by protamine sulphate (4·5 mg. per kilogram of body weight).

In our experience, repair of uncomplicated secundum type defects under hypothermia is a reliable method which allows assessment and accurate suture under vision.

The usual time required for suture of small defects is five minutes and for larger defects in the vicinity of seven minutes. The experience of this unit from November, 1957, is shown in Figure I and Table III.

For complicated and poor risk cases, the cardio-pulmonary by-pass has been used. The "Mark" screen oxygenator has been found a satisfactory apparatus, which is easy to handle. A high flow (in the region of 2·4 litres per square metre of body surface) has been used (Kirklin, 1957).

Cardio-Pulmonary By-Pass for Inferior Defects.

Repair of atrial septum primum and the atrio-ventricularis communis defects is possible only by the use of the by-pass. Sufficient time is available for accurate placing of the sutures in a dry field, and the hazards of incomplete closure, valvular incompetence and heart block are less likely. In this series, cardiac arrest during the period of by-pass was initially induced by the Melrose technique with potassium citrate solution diluted to 2·5% with arterial blood, and the arrested heart was immediately opened and decompressed (Melrose, 1955). In more recent cases, a bloodless surgical field has been attained by intermittently clamping the ascending aorta for periods up to three minutes, at the end of which time the clamp is released for 15 seconds to allow a coronary circulation, and reapplied. This method appears to be much safer, as there has been no interference with conduction. It has the added advantage that valve competence is tested as the stitches are placed. Cardiac arrest by citrate has now been abandoned.

In the first patient operated upon the heart was not arrested. A patch was inserted over the defect with difficulty in an obscure field. Closure was incomplete, and a severe degree of tricuspid valve incompetence resulted.

The danger of attempting closure of primum defects under hypothermia, a technique which requires adherence to a rigid time limit, is exemplified by the following case:

CASE I.—The patient was a girl, aged 19 years, with a large atrial septum primum defect and no mitral incompetence. This patient before operation was considered to have a septum secundum lesion, and the true diagnosis of septum primum defect was made at operation. The defect was repaired by running sutures between the lower margin of the defect and the top of the ventricular septum. Her initial recovery was uneventful, but she died a month later after the sudden development of cardio-respiratory distress. The post-mortem examination revealed that the sutures had cut through the anterior leaflet of the mitral valve, which had been inadvertently transfixed by a suture near its base during the repair. The defect had reopened and was complicated by acute mitral incompetence.

Technical Considerations in the Repair of Inferior Septal Defects.

Before heparinization, the anatomy of the defect and the presence of regurgitation through the valves are assessed with a finger in the atrium. The caval cannulæ for by-pass are so placed that they will not interfere with the operation field. The size of the defect and the presence of valvular deformity are reviewed when the patient is on total by-pass with the atrium opened.

The following measures have been found helpful:

1. The reflections of the thick lower margin of the atrial septal defect on to the top of the ventricular septum in front and behind are defined with sutures.

2. If there is no valvular deformity and the defect is small, repair can be accomplished by direct suture with the use of interrupted and running threads placed between the atrial rim and the top of the ventricular septum. To avoid the conduction bundle, the anterior sutures are placed in the fibrous ring to the left of the mid-line.

TABLE I.

Royal Alexandra Hospital for Children, January, 1947, to December, 1958: Analysis of Atrial Septal Defects Found Post Mortem.[1]

Type of Defect.	Number.	Age.	Cause of Death.	
			Cardiac.	Non-Cardiac.
Secundum.	26	Limits: 4 days to 1 year 10 months. Average: 14 weeks.	24	2
Primum and partial atrio-ventricularis communis.	6 (Mongoloid patients, 2)	Limits: 4 days to 13 years. Average: 4 years and 5 months.	5	1
Complete atrio-ventricularis communis.	17 (Mongoloid patients, 7)	Limits: 1 month to 26 months. Average: 6 months.	16	1

[1] Total number of deaths from congenital heart disease, 213; total number of deaths from atrial septal defect, 49.

3. If there is no valve deformity, but the defect is large and suture is possible only with tension, the defect is closed by a patch of woven "Teflon". This patch is inserted, after fixation at each end, by a series of sutures defining the top of the ventricular septum and the free margin of the atrial septal defect. In this manner defects can be closed without tension, with less danger of heart block, with less risk of valvular deformity and with less chance of recurrence.

4. If, besides the interatrial foramen, there is a cleft in the mitral or tricuspid valves, the lesion is a partial atrio-ventricularis communis defect. The clefts are repaired before closure by carefully placed interrupted sutures, care being taken not to include the chordæ tendinæ. The defect is usually closed with a patch in the manner described above.

CASE II.—The patient was a boy, aged 14 years. He was without symptoms, and was found to have a systolic murmur in the second left intercostal space and a diastolic murmur at the apex. There was Grade I cardiomegaly. The electrocardiogram showed left axis deviation and right bundle branch block. Cardiac catheter studies revealed a 2·4: 1·0 left-to-right shunt at atrial level and a normal pulmonary artery pressure. At operation, atrio-ventricularis communis defect with a split mitral valve was repaired by suture of the cleft valves, and the defect was closed by insertion of a patch under the by-pass. On restarting the heart, tricuspid incompetence was noticed on the monitor screen. The right atrium was reopened under the by-pass and one suture was removed from the tricuspid leaflet. This relieved the incompetence. At post-operative follow-up examination the patient was found to be active and well. His heart was without any murmurs and was normal in size.

5. As already defined, a complete atrio-ventricularis communis defect is one in which there are complete clefts

in both the septal cusp of the tricuspid valve and the anterior cusp of the mitral valve. The defects in the atrial and the ventricular septum abut on each other. This is one of the most intricate, difficult and dangerous intracardiac defects to cure. Correction is possible only if the ventricular septal defect is small, and if there is some fusion of adequate valve leaflets to the top of the ventricular septum. The valve rings are drawn to each other and to the top of the ventricular septum by appropriate sutures so as to give proper seating to the mitral and tricuspid valves. This permits careful suture of the clefts without tension. The valve leaflets are sutured to the top of the ventricular rim, sometimes through the

TABLE II.

Surgery of Atrial Septal Defects, Royal Prince Alfred Hospital, May, 1959.

Technique.	Type of Lesion.	Number of Cases.	Number of Deaths.
Hypothermia ..	Primum	3	1
	Secundum	33	2
By-pass	Primum	2	0
	Partial atrio-ventricularis communis.	5	0
	Atrio-ventricularis communis ..	2	2
	Secundum	7	1 (late)
Total ..	.. ..	52	6

intermediary of a horizontally placed patch, to obliterate any residual ventricular septal defect. The residual interatrial communication, which is now essentially a septum primum defect, is closed with a patch. Closure by direct suture is considered only in small and well-defined defects. In our experience, suture is inadequate.

Results of Surgery.[1]

Superior Defects.

In the series of 33 patients with secundum defects repaired under hypothermia there were two deaths. These occurred early in our experience, one from ventricular fibrillation, one from sudden tachycardia, the nature of which is doubtful. There was one later death in the seven atrial secundum defects repaired under by-pass. This case was one of Lutembacher's syndrome, and the patient died a month after operation with severe mitral regurgitation. Atrial defects repaired under the by-pass included those of serious hazard complicated by congestive heart failure, serious pulmonary venous anomalies, septum primum defect and atrio-ventricularis communis defect. These formed part of a series of 50 intracardiac operations performed for a variety of congenital and acquired heart lesions (Table III).

Inferior Defects.

There were 10 cases of inferior defects, comprising three of septum primum, five of partial atrio-ventricularis communis and two of complete atrio-ventricularis communis.

Two of the patients with primum defects were operated on successfully under the by-pass, and one unsuccessfully under hypothermia. This last patient died six weeks after operation from severe mitral regurgitation and reopening of the defect, as was mentioned earlier. One of the by-pass patients was first explored under hypothermia, and only later was the defect successfully closed under the pulmonary by-pass. In all three cases repair was by direct suture, and the result in the survivors is excellent.

The five partial atrio-ventricularis communis defects with clefts of the mitral valve were all successfully repaired under the by-pass. All these patients have some degree of incompetence. This is severe in three cases in which the cleft valve was not sutured, and mild in two cases in which suture was performed. The defect was repaired by a patch in two cases and by suture in three. In the case in which the valve was sutured and a patch inserted, an excellent result was obtained with minimal mitral imcompetence. In the other patient (the first operated upon in a field obscured by blood) there is a residual defect with both mitral and tricuspid regurgitation. Of the three cases in which the defect was repaired by direct suture, the result in one is good, but in two others there is tricuspid regurgitation.

The results emphasize the necessity for careful reconstruction without tension at the suture lines, for the valves are easily deformed.

The two patients with complete atrio-ventricularis communis defect have both died, one at operation and the other, unfortunately, from accident after initial recovery.

CASE III.—The patient was a girl, aged seven years, with an atrio-ventricularis communis defect. Her admission to the Hallstrom Institute of Cardiology was at the age of two and a half years with congestive heart failure, at which time the most significant cardiac findings were noted to be a systolic thrill and murmur at the apex and Grade II cardiac enlargement, mainly of the left atrium and left ventricle. In 1956, by cardiac catheterization a moderate left-to-right shunt at atrial level with moderate pulmonary hypertension was verified. Her condition was precarious in the ensuing years, the enlargement of the heart progressing to Grade IV in 1959. The electrocardiogram at this time showed elevation of the *P* wave, left axis deviation and right bundle branch block, all of which were confirmatory of an atrio-ventricularis communis lesion. At operation on January 20, 1959, under by-pass with heart arrested

TABLE III.

Intracardiac Surgery with By-Pass, Royal Prince Alfred Hospital, November, 1957, to May, 1959.

Disease Treated.	Number of Cases.
Ventricular septal defect	19
Atrial septal defect	18
Fallot's tetralogy	2
Infundibular stenosis	4
Aortic stenosis	5
Miscellaneous	2
Total	50

(potassium citrate 2·5% solution), the split mitral and tricuspid valves were sutured carefully together and to the deep notch in the top of the septum. The moderately sized inferior atrial septal defect was sutured to the top of the ventricular septum. When the aortic clamp was released to allow coronary circulation and resumption of the heart beat, there was temporary ventricular fibrillation, which was caused to revert to sinus rhythm by electrical defibrillation (180 volts for 0·1 second). The heart was decompressed before the rhythm was reversed—the right atrial chamber by releasing the vena caval tapes and going on to partial by-pass, and the left atrium by incision of the atrial appendix. The post-operative course was uneventful. The valves were competent clinically. Unfortunately, on removal of the intercostal drainage tube some days later, pneumothorax developed. During insertion of an intercostal catheter under local anæsthesia (lignocaine, 2% solution), fits developed and were followed shortly afterwards by cardiac arrest. Despite immediate restoration of the circulation, the patient died seven days later from the effects of anoxic brain damage.

Summary.

Some of the pathological features of a series of atrial septal defects have been reviewed briefly.

The principles governing the present practice of surgical repair of primum and secundum defects at this unit have been presented.

[1] Since this paper was delivered, the total number of atrial septal defects repaired by the techniques described has reached 86, and 90 intracardiac operations have been performed with the use of the cardiac by-pass and heart-lung machine.

The results of treatment in 10 cases of ostium primum and atrio-ventricularis communis defects are presented, and the surgery is critically discussed in the light of this experience.

Acknowledgements.

The work reported represents the combined efforts of surgeons and physicians of Royal Prince Alfred Hospital. In some of the earlier cases included the operations have been performed by Mr. F. Mills, and Mr. P. Tomlinson. The post-mortem records and the pathological material from the Royal Alexandra Hospital for Children were made available through the courtesy of Dr. R. D. K. Reye. The anæsthetics were administered by Dr. Jeanne Collison and Dr. Bruce Clifton and their staff.

References.

BLOUNT, S. G., BALCHUM, J., and GERSIN, I. (1956), "Persistent Ostium Primum Atrial Septal Defect", *Circulation*, 13: 499.

KIRKLIN, J. W., PATRICK, R. T., and THEYE, R. A. (1957), "Theory and Practice in the Use of a Pump Oxygenator for Intra Cardiac Surgery", *Thorax*, 12: 93.

MELROSE, D. G., BENTALL, H. H., BAKER, J. B., and DREYER, B. (1955), "Elective Cardiac Arrest", *Lancet*, 2: 21.

STUDY IN THE EFFICIENCY OF VACCINATION AGAINST INFLUENZA IN TWO EMPLOYMENT GROUPS IN MELBOURNE IN 1959.

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A LARGE number of studies, which have been recently reviewed by Francis (1959), have demonstrated that vaccination with influenza virus vaccine will materially reduce the incidence of infection with influenza viruses, and also reduce the severity of the illness in those who are infected, provided that the vaccine contains viruses antigenically similar to the epidemic strain, and that the dose of antigen is sufficient to give an adequate antibody response. Polyvalent vaccines have been developed recently, and these usually contain all the major antigenic subtypes of the Type A influenza viruses, and also representatives of the Type B and Type D influenza viruses. This type of vaccine is designed to give protection, not only against the current known circulating influenza viruses, but also against antigenically novel mutants which may arise in the future. Constant appraisal of the pattern of circulating influenza viruses and the pattern of antibody response to the various components is necessary, in order that adjustments making for greater efficiency of the vaccine may be made.

No change has yet been observed in the antigenic pattern of the epidemic Type A strains since the appearance of the A/Asia subtype in 1957, so that the efficiency of a polyvalent vaccine in giving protection against a changed pattern has yet to be demonstrated. This is a vital question in the study of protection against epidemic influenza, because, if it is confirmed that recycling of antigenic patterns occurs, as was suggested by Davenport and Hennessy (1958), then a major change of the future may be a recurrence of the subtype of influenza virus which was responsible for the 1918-1919 pandemic.

In the meantime, studies continue to determine the value of periodic vaccination to protect the population against epidemic or sporadic infection with the known influenza viruses. The true protective value of vaccination is often confused, because a large number of other viruses are able to cause respiratory tract infection, and the more severe cases of these other illnesses are often confused with influenza in the absence of laboratory studies. Fortunately, the techniques for isolating influenza viruses, and for testing for antibodies against both S (soluble, type-specific) and V (virus, strain-specific) antigens have become very efficient, and it is now possible to detect fairly accurately the date of onset and offset of epidemic influenza in a region served by a virus laboratory. Estimates of efficiency of vaccination should be restricted to the periods when it can be shown that the subjects studied could have been exposed to influenza.

Laboratory studies (Warburton, 1960) indicate that epidemic influenza was not present in Australia in 1958, and so no attempt was made to estimate protection rates in trials in Melbourne in that year. However, there was a widespread epidemic of A/Asian influenza in Australia in 1959, and the experience of respiratory tract infection of the employees of two large organizations was studied to determine the efficiency of the polyvalent influenza virus vaccine under field conditions.

Materials and Methods.

The survey was carried out on volunteers among two employment groups in Melbourne. One group was formed from the staff of a large Commonwealth department, the other group consisted of the employees of the City Authority. Both groups contained office and outside workers.

Vaccination against influenza was carried out as follows. Subjects who had been vaccinated in the previous year were given a single dose of vaccine. Those who had not been vaccinated previously were given the primary course of two doses. In Population A, the initial dose or the single booster dose of vaccine was given on April 2, and the second dose of vaccine was given on April 30. In Population B, the initial dose of vaccine or the single dose was given during the week April 16 to 20, and the second dose was given during the week May 1 to 5.

Commonwealth Serum Laboratories polyvalent influenza virus vaccine was used, each dose of 1 ml. containing the amounts indicated of the following antigens:

Type	Strain	Potency
Influenza virus A2	(A/Excell/57)	200 CCA units
Influenza virus A1	(A/WA/56)	50 CCA units
Influenza virus A	(PR 8)	50 CCA units
Influenza virus A-swine		50 CCA units
Influenza virus B	(B/Tas/53)	150 CCA units
Influenza virus D	(Sendai)	50 CCA units

In December, 1959, all employees were asked to supply details of respiratory tract illnesses by completion of a form which requested the following details for the preceding twelve months.

1. The number of attacks of influenza. The month of the attack or attacks. The duration of absence from work, and whether the illness was diagnosed by a medical attendant.

2. The number of colds or other respiratory illnesses. The month of the attack or attacks. The duration of absence from work, and whether the illness had been diagnosed by a medical attendant.

3. The history of previous influenza immunizations. The month of injections, the number of injections, and whether any adverse reactions had followed the administration of the vaccine.

To assess the data received, the subjects were divided into two groups, as follows. Group I, the vaccinated group, contained the individuals considered to be adequately immunized. They had had either a single booster dose of vaccine in 1959 following on two doses in the preceding year, or had had two doses of vaccine in 1959. Group II, the not-vaccinated or incompletely vaccinated group, consisted mainly of people who had not been previously vaccinated. However, this group contained a few individuals who had been vaccinated in 1958, but not in 1959, or had not been previously vaccinated and did not complete the two injections in 1959.

The year 1959 was considered a satisfactory period to examine the efficacy of the vaccine in preventing influenza,

as it is known from laboratory studies that there was a widespread epidemic of Asian influenza in Australia in that year. We have an accurate knowledge of the duration of the epidemic in Melbourne based on virus studies carried out at the Epidemiological Research Unit at Fairfield Infectious Diseases Hospital, whose Director, Dr. A. A. Ferris, has allowed us to use his information in compiling this report.

Population A returned 1427 forms for examination. There were 487 subjects in the vaccinated group and 896 in the not-vaccinated or incompletely vaccinated group; 44 forms were not considered, because the data were incomplete. From Population B, 561 forms were received. There were 355 subjects in the vaccinated group and 197 subjects in the not-vaccinated or incompletely vaccinated group; 9 forms were not considered because of incomplete data.

The number of days of absence in each month from January to December were calculated for both influenza and other respiratory illnesses. From these figures it was possible to calculate the time lost from work per person per month in each group for both influenza and other respiratory illnesses. We have taken the number of days of illness severe enough to necessitate absence from work as the measure of the amount of influenza and other respiratory diseases present in each month, and compared these for the vaccinated and control groups in each population, on the common basis of time lost per person per month, to assess any protection due to vaccination.

Results.

The results have been considered from two aspects: (i) days lost by each employee from illnesses considered to be influenza; (ii) days lost by each employee from all respiratory tract illnesses including influenza. The results for each population for each month are shown in the histograms (Figures I, II, III and IV).

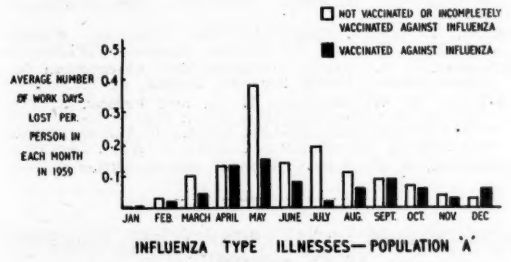

NOT VACCINATED OR INCOMPLETELY VACCINATED AGAINST INFLUENZA
VACCINATED AGAINST INFLUENZA
AVERAGE NUMBER OF WORK DAYS LOST PER PERSON IN EACH MONTH IN 1959
0·5
0·4
0·3
0·2
0·1
JAN. FEB. MARCH APRIL MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC.
INFLUENZA TYPE ILLNESSES—POPULATION 'A'

FIGURE I.

Influenza-type illnesses, Population A.

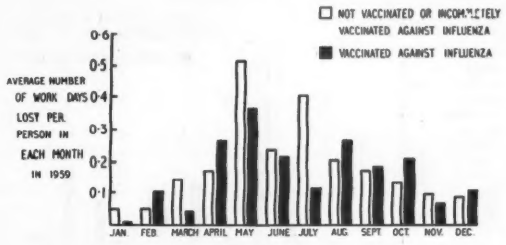
A significant protective effect against influenza was observed in the vaccinated groups in Population A and Population B during the month of May, the protection rates being 60% and 61% respectively. In that month, in Population A respiratory illnesses other than influenza accounted for 0·2 day per person in the vaccinated group and 0·13 day per person in the control group, and in Population B respiratory infection other than influenza accounted for 0·1 day per person in the vaccinated group and 0·16 day per person in the control group. These figures appear to be independent of vaccination.

Protection against influenza was also observed in Population A in July, when the protection rate was 89%. In that month, in Population A respiratory illness other than influenza accounted for 0·09 day per person in the vaccinated group and 0·21 work day per person in the control group, and this difference is also significant. The protection rate against other respiratory illnesses is 57%.

In Population B, in July the incidence of both influenza and other respiratory illnesses was markedly lower than in Population A, and there was no significant difference between the incidence in the vaccinated and the control group.

Discussion.

The influenza epidemic had begun in Melbourne before vaccination was completed in either population; however, similar protection rates were established in both groups for May, the month in which the majority of cases of influenza occurred. The virus laboratories of the Epidemiological Research Unit at Fairfield Infectious Diseases Hospital attempted virus isolation from the wide variety of cases of respiratory tract illnesses admitted there throughout the year, and we consider that the rate of isolation of influenza viruses at that hospital parallels the rate of occurrence of those viruses in the population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VACCINATED AGAINST INFLUENZA
AVERAGE NUMBER OF WORK DAYS LOST PER PERSON IN EACH MONTH IN 1959
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0·5
0·4
0·3
0·2
0·1
JAN. FEB. MARCH APRIL MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC.

FIGURE II.

Influenzal and other respiratory illnesses, Population A.

of Melbourne. During 1959, influenza viruses were isolated only between March 19 and June 26, and Figure V demonstrates that most of the influenzal infections occurred during May. All influenza viruses isolated were of the A/Asian type.

Although a large number of field trials have demonstrated that a protection rate against influenza averaging 75% can be expected for an adequately immunized population, it is very likely that our results show a lower rate because the epidemic of influenza was well under way

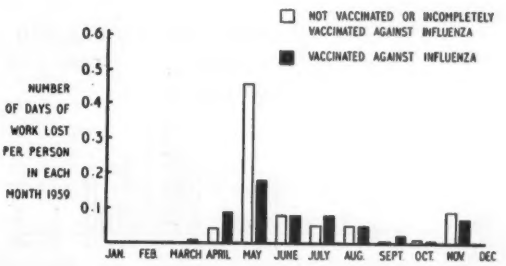

NOT VACCINATED OR INCOMPLETELY VACCINATED AGAINST INFLUENZA
VACCINATED AGAINST INFLUENZA
NUMBER OF DAYS OF WORK LOST PER PERSON IN EACH MONTH 1959
0·6
0·5
0·4
0·3
0·2
0·1
JAN. FEB. MARCH APRIL MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC.
INFLUENZAL TYPE ILLNESSES—POPULATION 'B'

FIGURE III.

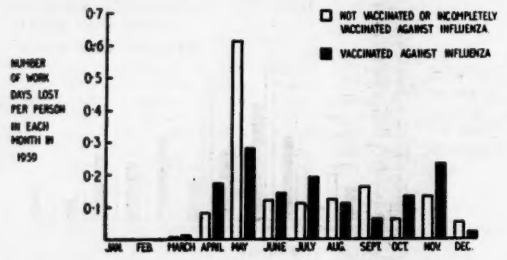
Influenza-type illnesses, Population B.

before vaccination was completed. The influenza epidemic occurred unusually early throughout Australia in 1959. In Perth, a survey by Mathieson (1959) of the incidence of influenza between vaccinated and unvaccinated public servants showed a protection rate of 58%, and here also the epidemic had begun before vaccination was completed.

The finding of apparently substantial protection in the vaccinated in Population A during July was a surprise, as there was no evidence of circulation of Type A or Type B influenza viruses in that month. Neither the Epidemiological Research Unit nor the W.H.O. Surveillance Laboratory at the Commonwealth Serum Laboratory isolated any influenza viruses during July. It is also unlikely that there were any localized outbreaks of Type B influenza viruses from which specimens for virus isolation were not received, because routine examination of blood-bank sera throughout 1959 for complement-fixing antibodies showed no evidence of recent infection with Type B viruses in Melbourne.

It is possible that the difference in incidence between the vaccinated and unvaccinated groups, although statistically significant, was fortuitous. On the other hand, it may be explicable in terms of a localized epidemic of infection with hæmadsorption viruses, which were known to be present in Melbourne in July. Hæmadsorption viruses are antigenically related to the Type D (Sendai) influenza virus; this is a component of the polyvalent influenza virus vaccine, which could be expected to have protective value against them.

Hæmadsorption viruses may cause illness in adults resembling influenza (McKinney, England and Froede,



INFLUENZAL AND OTHER RESPIRATORY ILLNESSES—POPULATION 'B'

FIGURE IV.

Influenzal and other respiratory illnesses, Population B.

1959) or resembling the ordinary cold (Andrewes, 1959). Type I hæmadsorption viruses were isolated at the Epidemiological Research Unit from sporadic cases of croup in children in 1959 in every month from May to December, and Type II hæmadsorption viruses were isolated in July, September, October, November and December. The Sendai virus is very closely related antigenically to the

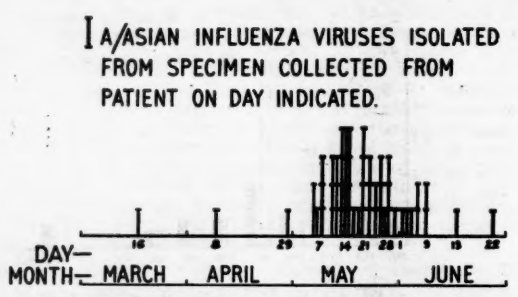

I A/ASIAN INFLUENZA VIRUSES ISOLATED FROM SPECIMEN COLLECTED FROM PATIENT ON DAY INDICATED.
DAY—
MONTH— MARCH APRIL MAY JUNE

FIGURE V.

Temporal distribution of Asian influenza epidemic in Melbourne in 1959, as measured by isolation of viruses from patients with respiratory tract disease admitted to Fairfield Infectious Diseases Hospital.

Type II hæmadsorption virus (Chanock *et alii*, 1958) and it has recently been proposed by the Virus Sub-Committee of the International Nomenclature Committee (Andrewes, Bang, Chanock and Zhdanov, 1959) that both these viruses be included as members of Type I of a new sub-group of myxoviruses called the para-influenza viruses. The antigenic overlap between Type I hæmadsorption virus and the Sendai virus is less pronounced (McKinney *et alii*, 1960), and the Virus Sub-Committee has recommended that Type I hæmadsorption viruses should become Type III para-influenza viruses.

Summary.

A comparison of the incidence of influenza necessitating absence from work in the employees of two large organizations in Melbourne demonstrated a protection rate during the month of May of 60% for those vaccinated with polyvalent influenza virus vaccine. Laboratory studies indicate that May was the month in which the majority of A/Asia influenza infections occurred in Melbourne.

Influenza occurred unusually early throughout Australia in 1959, and the epidemic had already begun before vaccination was completed, so that the protection rate is probably less than it would have been if vaccination had been carried out earlier.

A protection rate of 89% against influenza-like infections was also observed in July in one of the populations studied, although there is no laboratory evidence to indicate the presence of true influenza viruses in Melbourne in that month. We postulate that these people may have been infected with either Type I or Type II hæmadsorption viruses, and that the vaccinated were protected by the Type D (Sendai) influenza virus component of the vaccine.

Acknowledgements.

We gratefully acknowledge the cooperation in this study of the Deputy Director of Taxation and his staff, and of Dr. P. Gilbert, Chief Medical Officer of the Melbourne City Council. We thank Dr. A. A. Ferris, Dr. M. M. Nelson and Mr. F. Lewis, of the Epidemiological Research Unit at Fairfield Hospital, for the information supplied from their studies. We also thank Dr. P. L. Bazeley for his interest and advice in this study.

References.

ANDREWES, C. H. (1959), "The Common Cold and Other Minor Respiratory Infections", *Brit. med. Bull.*, 15: 221.

ANDREWES, C. H., BANG, F. G., CHANOCK, R. M., and ZHDANOV, V. M. (1959), "Para-Influenza Viruses 1, 2 and 3: Suggested Names for Recently Described Myxoviruses", *Virology*, 8: 139.

CHANOCK, R. M., PARROTT, R. H., COOK, K., ANDREWS, B. E., BELL, J. A., REICHELDERFER, T., KAPIKIAN, A. Z., MASTROTA, F. M., and HUEBNER, R. J. (1958), "Newly Recognized Myxoviruses from Children with Respiratory Disease", *New Engl. J. Med.*, 258: 207.

DAVENPORT, F. M., and HENNESSY, A. V. (1958), "The Clinical Epidemiology of Asian Influenza", *Ann. intern. Med.*, 49: 493.

FRANCIS, T. (1959), "Influenza", in "Viral and Rickettsial Infections of Man", 3rd Edition, Lippincott, Philadelphia.

MATHIESON, J. B. (1959), "Influenza and Absenteeism in the Commonwealth Public Service", *Health*, 9: 125.

MCKINNEY, R. W., ENGLAND, B. L., and FROEDE, S. (1959), "Studies with Hæmadsorption Virus Type 1. Recovery from Two Cases of Influenza-Like Disease in Military Personnel and Related Investigations", *Amer. J. Hyg.*, 70: 280.

WARBURTON, M. F. (1960), personal communication.

TRIMEPRAZINE ("VALLERGAN"): ITS ASSESSMENT AS AN ANTIPRURITIC.

By ERIC H. TAFT, M.R.C.P. (Edinburgh), D.D.M. (Sydney),
BRIAN R. ENTWISLE, D.D.M. (Sydney,
AND
RUSSELL LANGLEY, D.D.M. (Sydney),
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ITCHING is the common denominator of a great number of dermatoses, and a drug able to control pruritus, irrespective of ætiology, would fill an important place in the treatment of skin diseases.

Recent enthusiastic reports by Anderson and Chalmers (1959), London (1959), and others have claimed that a phenothiazine derivative, trimeprazine, is an effective antipruritic when taken orally. Trimeprazine ("Vallergan") is regarded pharmacologically as being intermediate between promethazine ("Phenergan") and chlorpromazine ("Largactil"). The above-mentioned reports are open to criticism on a number of grounds, and it was thought that a clinical trial using adequate controls and subject to statistical analysis would help to evaluate this new drug.

TABLE I.

Condition.	Total Number of Cases.	First Course of Therapy.	Status of Patients.			Second Course of Therapy.	Status of Patients.		
			Improved.	Unchanged.	Worse.		Improved.	Unchanged.	Worse.
Atopic dermatitis	14	Trimeprazine (9) Placebo (5)	6 3	3 2	— —	Placebo (9) Trimeprazine (5)	6 —	2 5	1 —
Discoid eczema	19	Trimeprazine (9) Placebo (10)	5 5	2 4	2 1	Placebo (9) Trimeprazine (10)	3 3	3 3	3 4
Localized neurodermatitis.	9	Trimeprazine (5) Placebo (4)	3 2	1 2	1 —	Placebo (5) Trimeprazine (4)	1 1	3 3	1 —
Miscellaneous dermatoses.	13	Trimeprazine (9) Placebo (4)	3 1	4 3	2 —	Placebo (9) Trimeprazine (4)	3 1	6 3	— —

Method.

Consecutive patients attending the skin out-patient clinic at Prince Henry's Hospital, who complained of pruritus, were examined by one or other of us and admitted to the trial. No selection was made as to sex or age. Patients under treatment at the beginning of the trial continued with the applications they were using, whilst new patients were ordered bland non-specific local applications only.

A clinical clerk entered the name of each patient into a book and distributed the tablets. These consisted of either trimeprazine ("Vallergan"), 10 mg., or a placebo composed of lactose and starch. The tablets were all coloured blue and of identical appearance. The patients received the tablets in a random manner, but generally alternate patients received either the drug or the placebo. The patients did not know that a clinical trial was being conducted, and no comment was made concerning the existence of the trial or the value of the tablets by the clerk, doctor or any member of the medical or nursing staff. After a period of treatment, a "cross-over" of tablets—unknown to both patient and doctor—was made by the clerk.

TABLE II.

Course of Therapy.	Status of Patients.		
	Improved.	Unchanged.	Worse.
First course: Trimeprazine (32) .. Placebo (23)	17 11	10 11	5 1
Second course: Placebo (32) .. .. Trimeprazine (23) ..	13 5	14 14	5 4

Each patient was examined at regular intervals throughout the trial by the same doctor. The duration of the trial was five months, and the average duration of treatment was three weeks with each tablet. Whilst the average dose was one tablet three or four times a day, equivalent to 30 or 40 mg. of active ingredient, a few patients received as many as six tablets daily, equivalent to 60 mg. of active ingredient.

Assessment was based on the patient's opinion of his pruritus at the end of the first course of treatment compared with this symptom before treatment had commenced. He was also assessed at the end of the second course compared with his status at the end of the first course of treatment. The condition as assessed was divided into three categories: (i) improved; (ii) unchanged; (iii) worse. Thus, it would have been necessary for a patient to improve still further after the first course of treatment to achieve a rating of "improved" in the second course. If he merely maintained his improved state, he would be rated as "unchanged" for the second course.

Results.

A total of 72 patients, whose ages ranged from four to 88 years, were entered into the trial. Because they failed to attend again, three patients were deleted from the series after the initial consultation and issue of tablets, and 14 after the cross-over of tablets. Of the latter 14, three out of six had improved with trimeprazine, whilst five out of eight had improved with the placebo. The series therefore included 55 patients. The results are shown in Table I and summarized in Table II.

Included in the nine cases of localized neurodermatitis were two cases of ano-genital pruritus. The 13 cases classified as miscellaneous dermatoses included stasis dermatitis (2), senile pruritus (5), psychogenic pruritus (1), erythroderma (2) and dermatitis herpetiformis (3).

TABLE III.

Course of Therapy.[1]	Improved.		Unchanged.		Worse.	
	Observed.	Expected.	Observed.	Expected.	Observed.	Expected.
First course[1]: Trimeprazine .. Placebo ..	17 11	16·3 11·7	10 11	12·2 8·8	5 1	3·5 2·5
Second course[2]: Placebo .. Trimeprazine ..	13 5	10·5 7·5	14 14	16·3 11·7	3 4	5·2 3·8

[1] Observed $\chi^2 = 2 \cdot 60$ (not significant); two degrees of freedom.
[2] Observed $\chi^2 = 2 \cdot 25$ (not significant); two degrees of freedom.

These results were analysed statistically by Dr. G. Gregory. The two courses of therapy were considered separately, and in each case tested for a significant difference in the classification of patients (improved, unchanged, worse) after trimeprazine and the placebo. If there was no difference, the numbers in each classification would be approximately proportional to the number of patients undergoing the particular treatment. Comparison of these expected values with the value observed by means of a χ^2 test yielded non-significant results in both cases, as shown in Table III. Dr. Gregory thought that the conclusion of "no difference" was the only reasonable one on the basis of this evidence, no matter what test was used.

Clinical evaluation of trimeprazine and the placebo in the 55 cases showed that (i) trimeprazine was more effective than the placebo in 12 cases, (ii) the placebo was more effective than trimeprazine in 10 cases, (iii) there was no real difference in effectiveness between trimeprazine and placebo in 33 cases.

In the trial, side effects were observed as shown in Table IV.

Comment.

In this series of 55 patients, under the conditions of a double-blind clinical trial with cross-over of tablets, there was no indication that trimeprazine was superior to a placebo tablet as an antipruritic.

It is to be noted that this result contradicts the reports cited above. This may be due to the fact that Anderson and Chalmers (1959) had no cross-over of tablets and insufficient patients in the control group, whilst in London's (1959) trial there were insufficient patients in the cross-over group.

Recently, Bartholomew (1960) has commented on the limited usefulness of inadequately controlled trials of drugs, a criticism with which we are strongly in agreement. This comment is particularly relevant to the evaluation of a symptom such as pruritus.

The large number of patients improved by the placebo tablets in this trial agrees with the findings of Beecher (1955), who, analysing the results in 1082 patients, has shown that the effectiveness of a placebo was of the order of 35% whatever symptom was studied.

TABLE IV.

Side Effect.	Number of Patients.	
	Trimeprazine.	Placebo.
Drowsiness	2	6
Dizziness	1	—
Temporary disorientation	1	—
Dry mouth	—	1

Summary.

Trimeprazine ("Vallergan") has been reported as being an effective antipruritic when given orally irrespective of the ætiology of the symptom.

A controlled clinical trial, which was double-blind and used a cross-over technique, involving 55 patients is reported, and the results are subjected to statistical analysis. There was no indication that, in the doses used, trimeprazine was more effective as an antipruritic than a placebo tablet.

Toxic symptoms were not frequent, and even the placebo was responsible for some unpleasant side effects.

Acknowledgements.

We are indebted to Dr. G. Gregory, Department of Statistics, University of Melbourne, for his analysis of the results, and wish to thank Dr. Garry Bennett, Dr. H. H. Jackson and Dr. C. Lancaster, Sister H. Harris and Mr. George Munro for their help in conducting the trial. We also wish to thank Mr. K. C. Curnick, of Messrs. May & Baker (Aust.) Ltd., for the supply of all tablets.

References.

ANDERSON, T. E., and CHALMERS, D. (1959), "A Trial of Trimeprazine in Itching Dermatoses", *Brit. J. Derm.*, 71: 214.

BARTHOLOMEW, A. A. (1960), MED. J. AUST., 1: 556.

BEECHER, H. K. (1955), "The Powerful Placebo", *J. Amer. med. Ass.*, 159: 1602.

LONDON, I. D. (1959), "Double-Blind Evaluation of Trimeprazine", *A.M.A. Arch. Derm.*, 80: 220.

THE USE OF A PAPAIN SOLUTION OF APPROXIMATELY pH 3·0 IN Rh TESTING AND ATYPICAL ANTIBODY DETECTION.[1]

By J. A. ALBREY AND R. T. SIMMONS,

From the Red Cross Blood Transfusion Service (Queensland Division), Brisbane, and the Commonwealth Serum Laboratories, Melbourne.

FOR over fifteen years, blood group serologists have been striving to improve the accuracy of blood group determinations and methods employed in blood compatibility testing prior to transfusion. In two decades many "new" blood groups have been discovered, and blood groups thought to be simple have been shown to be extremely complex. In the laboratory, the full weight of serological thought has been directed to problems associated with hæmolytic disease of the new-born and to blood compatibility testing, to ensure that atypical antibodies are detected with speed and accuracy, not only in the central testing laboratories, but also in the smaller hospital laboratories.

It was shown many years ago in blood compatibility testing that the suspension of red cells in physiological saline mixed with the patient's serum detects the presence of agglutinating antibodies only, while non-agglutinating antibodies of the incomplete type, and equally dangerous, remain undetected. The incomplete or blocking Rh antibodies, found independently by Race, of London, and by Wiener, of New York, were shown to act as agglutinating antibodies in the presence of media of high protein content, and thus the use of 30% bovine albumin recommended by Diamond, of Boston, serum-albumin tests as described by one of us (R.T.S.) and plasma-albumin tests as described by Wiener, became accepted methods for incomplete antibody detection. The Coombs test, elaborated by Coombs, of Cambridge, employing an anti-human globulin serum, further increased the sensitivity of atypical antibody detection. The combined use of saline, albumin and antiglobulin tests is still the preference of the laboratory aiming at reliability of antibody detection. However, for ten years the use of proteolytic enzymes in blood group serology has increased, even though each enzyme possesses disadvantages as well as advantages.

The purpose of the present communication is to discuss the use and distinct advantages of a low pH activated papain solution in Rh testing and antibody detection. The use of a pH of 2·8 to 3·1, which stabilizes the papain after preparation, and of subsequent mixtures of papain and incomplete anti-Rh serum, permits Rh testing over extended periods, instead of its being limited to about 15 minutes after mixing, as in the past. Further, methods for using the papain solution in very sensitive techniques in antibody detection will be described. The advances reported here open the way for wider use of papain in blood group practice than ever before, and remove the most serious disadvantage in the use of papain and activated papain.

THE PROTEOLYTIC ENZYMES USED.

Proteolytic enzymes have been used in the following order.

Cholera Filtrates and Trypsin.

The use of proteolytic enzymes in blood grouping stems from the initial observation reported by Pickles (1946) that a cholera filtrate agglutinated sensitized Rh-positive cells suspended in saline. Morton and Pickles (1947) made a further advance when they demonstrated that a solution of the enzyme trypsin had a similar effect in that it also agglutinated Rh-positive cells sensitized with incomplete Rh antibody.

Papain.

Serologists thought of the possible uses of other proteolytic enzymes, and Kuhns and Bailey (1950) used 0·1% papain solution (from papaya or papaw) to sensitize test cells for titrating 25 incomplete anti-Rh sera. They found papainized cells to be satisfactory and more sensitive than the serum albumin or trypsin methods.

Ficin.

The use of ficin from the latex of the genus *Ficus* was suggested by Wiener and Katz (1951), and in their report they state that they obtained satisfactory results with cells treated with trypsin, papain and ficin in the detection of Rh antibodies and antibodies of other specificities. They issued a warning that ficin was dangerous to handle and that eyes should be protected.

The Antiglobulin Test on Enzyme-Treated Cells.

Unger (1951) found that an antiglobulin test on trypsinized cells was a sensitive method for the detection

[1] Read at the scientific session of the Australian Red Cross National Blood Transfusion Committee on November 20, 1959, at Melbourne.

of Rh antibodies. Vogt and Heistö (1953) compared eight methods for detecting Rh antibodies, and concluded that the use of papainized cells with a subsequent antiglobulin test was the most sensitive. They titrated 50 incomplete anti-Rh sera.

Activated Papain.

Stratton (1953) pointed out that papain required an activator for its reaction, and used L-cysteine hydrochloride for this purpose. He described a seven-minute slide test performed at room temperature with a 10% suspension of papainized cells for detecting all varieties of Rh antibodies. He observed that some reactions not due to Rh antibodies were due to anti-P, anti-Lewis, anti-Kell antibodies or to rare auto-antibodies. Few false-positive results were obtained, and the method was found to be accurate and speedy. The pH of the papain-activator mixture was raised to a predetermined level of 6·7 with the use of isotonic phosphate buffer. Stratton also observed that the method of red-cell collection had an effect on the strength of the reaction. Cells collected into glucose-disodium citrate solution had a higher degree of activity than cells collected as clotted or defibrinated blood. A serum which had a trypsin titre of 8 had a papain titre of 64 and an activated papain titre of 256. Goldsmith (1955) used non-activated papain in buffered saline at pH 7·3 for red-cell treatment in examining 3370 maternal sera for the detection of incomplete antibodies, and found that tests with papainized cells were more sensitive than tests in saline, 20% bovine albumin, antiglobulin and trypsin. Goldsmith considered that the papain tube technique was sensitive and reliable for routine use in the detection of incomplete Rh antibodies. Löw (1955) reported on the use of papain activated with cysteine in phosphate buffer at pH 5·4, and found that this pH was better than 7·3 in Rh testing. The tests were carried out in tubes incubated for two hours at 37° C., and the mixture consisted of incomplete anti-Rh serum, papain and 3% cell suspension. A condition laid down was that the anti-Rh serum-enzyme mixture must not be used more than four hours after being mixed. Stern, Busch and Buznitsky (1957) used L-cystcine hydrochloride activated papain of pH 6·4 to 6·7 in an enzyme cross-match test, and for the papainization of red cells in screening sera from 20,235 donors and from 6054 recipients for atypical antibodies. Tests were performed in tubes, and the tubes were incubated at 37° C. for 30 minutes and centrifuged. Anti-Rh, anti-A, anti-B and anti-K antibodies were demonstrated, also auto-agglutinins and cold agglutinins. Anti-Duffy antibody was not detected. The enzyme solution in the presence of serum was capable of proteolytic destruction of the antibody in 30 to 60 minutes. Haber and Rosenfield (1957) used a solution of ficin at pH 7·3 in a tube test for Rh-Hr isoimmunization studies and found it more sensitive than trypsin. They gave a warning of the danger of toxicity to mucous membranes by contact with ficin. The test-cell suspensions used were treated with a 1% solution of ficin. The ficin titre results approximated those obtained by the papain method, but they preferred ficin because of its stability. The solution is stable for one week at 4° C., and for many months at −20° C. Ficin was found useful for detecting Rh, Jk, Le and P antibodies. It destroyed the Fy^a and MNSs factors, but did not destroy the Kk factors.

Bromelain.

Lewis (1957) tested three enzymes, papain, ficin and bromelain (from pineapple pulp). Trypsin was excluded from the study because the phenomenon of reversible agglutination is a serious limitation to its use on a slide. Tests were made in a range of pH 5·4 to 8·4. Papain was most active at 5.4, and ficin and bromelain at 8·4. The test cells used for the detection of incomplete Rh antibodies were modified at 37° C. for 30 minutes, then washed and suspended in saline. Most tests were done in tubes, but some were done on warm tiles. It was found that all Rh antibodies reacted; there were slight increases in activity of anti-Le^a, anti-Le^b, anti-A, anti-B and anti-P, no change in anti-K, anti-Lu^a and less with anti-M and anti-N, while tests failed with anti-Fy^a. It was pointed out that enzyme treatment of red cells had the following advantages over standard methods of antibody detection: absence of rouleaux, abolition of the prozone phenomenon, saving on reagent costs (albumin and antiglobulin serum), saving on labour, and the speed and accuracy of such tests. Disadvantages include the overlapping of specific and non-specific agglutination, and enhanced sensitivity to non-specific cold agglutinins.

Activated Papain Slide Test.

Hekker, Klomp-Magnee, Krijnen and van Loghem (1957) tested 125,000 blood samples by a slide test using one drop of a 5% red-cell suspension, one drop of a cysteine hydrochloride activated papain solution at pH 6·2, and one drop of an incomplete anti-Rh serum with a titre of 128 to 512. After mixing, the slides remained for 15 minutes at room temperature and were then read macroscopically. These workers recommended the slide test for mass Rh typing. It was found that serum-papain mixtures deteriorated in 15 minutes, and the deterioration also occurred rapidly at −20° C. The activity could be restored by the addition of either fresh papain or fresh serum. It was considered that papain solutions with a pH of 5·4 to 6·4 were most suitable. In using a papain solution of pH 6·2, it was found that the addition of Rh-testing serum increased the pH to 6·5, which was regarded as a pH of choice for optimal Rh agglutination. Recurrent turbidity and formation of white precipitate necessitated centrifugation of the papain solution before use to avoid false-positive reactions. The papain solution deteriorated quickly at room temperature or in the ice box, but was satisfactorily stored at −20° C., or lyophilized, for six months. Race and Sanger (1958) summed up the value of papain by stating that the papain technique gave strong reactions with practically all Rh, Kell, Lewis, Kidd and P antibodies, while Duffy and the MNSs antibodies did not react at all.

Greenwalt (1959), at a meeting of the American Association of Blood Banks, presented examples of a number of antibodies which were unusual, because they were found in individuals with no known previous exposure to the antigen, and were detected only or at best in the cysteine-activated papain system as described by Löw (1955). The specificities of the antibodies described were anti-Rh_o(D), anti-rh′(C) and anti-rh″(E).

In the methods involving activated papain described above, use is made of solutions buffered at pH values varying between 5·4 and 6·7. Papain is most active in the pH range 5·0 to 6·0, whereas Rh antibodies have been found to lose their activity below pH 6·5, so that pH values chosen for the various papain solutions represent a compromise. At any of the pH values selected, cysteine in solution is susceptible to atmospheric oxidation. It is a much more stable compound as the hydrochloride, which forms a very acid solution. As a result of initial work by one of us (J.A.A.) in Brisbane, in which activated papain solutions of varying pH values below 6·2 were investigated, it was found that at pH 2·8 to 3·1 solutions were stable at 5° C. for approximately one month, but were not suitable for use with a saline suspension of cells. If the cells are suspended in the glucose-citrate solution, as described by Simmons and Graydon (1945), at a concentration of 20% to 25%, good results are obtained.

Materials and Methods.

Preparation of Activated Papain Solution pH 2·8 to 3·1.

The solution is prepared according to the method of Löw (1955), except that the final pH is 2·8 to 3·1, and not 5·4 as specified by Löw. The details of preparation are as follows:

Two grammes of papain (Merck 1:350, or B.D.H.) are ground as a paste in a mortar with a minimum amount of M/15 phosphate buffer solution pH 5·4. The ground papain is washed into a flask with 100 ml. of the buffer solution, and then centrifuged to remove most of the undissolved papain. The supernatant is filtered through a (D5) clarifying filter pad. To the filtrate are added 10 ml. of 0·5M cysteine hydrochloride solution (freshly prepared), and the solution is diluted with buffer to 200 ml. The

solution is incubated to activate the enzyme for 1 hour at 37° C. The pH at this stage should be 2·8 to 3·1 and it should be checked. The clear papain solution is stored in small amounts at −20° C., but it also remains active and without the development of a white precipitate for some weeks at 5° C.

The reagents used are as follows: M/15 KH_2PO_4 contains 9·07 grammes per litre. M/15 Na_2HPO_4 contains 9·47 grammes per litre. Buffer solution of pH 5·4 is said to require 9·6 ml. of the potassium salt and 0·4 ml. of the sodium salt; however, in the present instance the proportions used were 9·7 ml. and 0·3 ml.

M solution of cysteine hydrochloride contains 157 grammes per litre (0·5M solution contains 1·57 grammes in 20 ml. of distilled water). The cysteine hydrochloride is used without neutralization, and should be freshly prepared.

Procedure.

In routine blood typing and antibody testing the low pH papain solution has been used in three ways.

Rh Testing by Slide Technique (Single-Stage).

When high-titre incomplete Rh antisera of different specificities are used in routine Rh testing, the serum is initially diluted with saline, and then with one, two or three volumes of activated papain solution according to the potency of the serum. Alternatively the saline diluent may be omitted, in which case a minimum of four volumes of papain diluent is desirable to keep the final pH below 4·0 to 4·5. If this is done, the serum will remain active for at least 10 to 14 days at 5° C. (By using two incomplete anti-Rh_o(D) sera stimulated by repeated transfusions, it has been found possible to dilute 1:150 to 1:200 with saline, and then to add a further equal volume of activated papain solution. This mixture remains active for as long as 30 days at 5° C.) In Rh testing, equal volumes of the serum-papain mixture and unwashed cells in glucose-citrate solution are mixed on a slide, and incubated at 37° C. for 10 to 15 minutes in moist chambers. Readings are made macroscopically. As with most Rh testing, the agglutination results after incubation at 37° C. are superior to those obtained at room temperature.

If the serum is not sufficiently potent to be diluted 1:5 with papain, it is often possible to use it as a routine testing serum by placing one drop of the undiluted serum on a slide, and adding one drop of activated papain solution and one drop of 20% to 25% cells in glucose citrate solution. The three drops are mixed and incubated for 10 to 15 minutes (or longer if necessary), and the result is read as before. Readings should be made while the slides are being gently tilted.

Antibody Detection by Slide Technique (Modified Two-Stage).

The most sensitive method is one that involves a two-stage technique, and is therefore used (a) in blood-grouping practice with sera containing less potent antibodies (anti-Kell, anti-e, anti-Kidd), and (b) as a rapid screening test in the detection and identification of antibodies using selected blood samples. One drop of a 20% to 25% suspension of unwashed cells is mixed with one drop of papain solution on a slide, and incubated at 37° C. for 10 minutes. During this first stage the pH of the mixture lies in the range 5·0 to 6·0, and rapid papainization is achieved. The actual pH value depends on the amount of serum or plasma included with the unwashed cell suspension. The rise in pH from about 3·0 to 5·0 or 6·0 is the result of the buffering effect of the cells, the glucose-citrate solution, the included serum or plasma and the phosphate buffer. After 10 minutes' incubation at 37° C., the slide and the moist container are removed from the incubator. One drop of serum is then added to the centre of the papain and cell mixture without any attempt at mixing. The slide is left untouched for two or three minutes at room temperature. Readings are made macroscopically.

Even greater sensitivity in the detection of some very weak antibodies may be achieved if the papain solution is diluted with an equal volume of glucose citrate solution immediately before use. The procedure is the same, except that in the first stage the incubation period at 37° C. is extended to 15 minutes.

Discussion.

The two-stage slide technique lends itself admirably to blood compatibility testing, especially for the detection of Rh antibodies, and in some instances such antibodies may be detected before they become evident with conventional methods in general use. However, it must be stressed, that, while the papain technique is rapid and reliable for detecting most incompatibilities, it cannot be depended on as a single method of compatibility testing. It has been shown to give strong reactions with practically all Rh, Kell, Lewis, Kidd and P antibodies, while Duffy and the MNSs antibodies generally do not react at all. Therefore, it can only supplement, or precede as a rapid screening test, the present methods of blood compatibility testing, such as the use of cells in glucose-citrate solution at room temperature, cells in 30% bovine albumin at 37° C., and the indirect Coombs test. The single-stage test is admirable for routine Rh testing. It has been shown that a cysteine hydrochloride activated papain solution of pH 2·8 to 3·1 eliminates the most serious disadvantages previously associated with the use of papain solutions in blood group serology—namely, the rapid deterioration of activity at all temperatures down to and including 5° C., and the very rapid destruction of Rh-agglutinating activity in mixtures of such sera and the papain solution. The present papain solution is stable for at least a month at 5° C., and remains entirely free of turbidity and precipitate. Mixtures of this activated papain and high-titre incomplete anti-Rh sera used at dilutions of 1:150 to 1:200 have remained active for one month at 5° C., thus opening the way for greater use of incomplete anti-Rh sera in Rh blood testing.

During the past year, 45,700 Rh tests have been performed on specimens from blood donors (many of whom, being regular donors, had previously been tested with complete anti-Rh_o(D) sera), and on specimens from pregnant women. No discrepancies were found, except that Rh_o(D) variants, not detected by complete anti-Rh_o(D), were, with two exceptions, revealed without recourse to the anti-human globulin test.

Possible sources of error in the use of a papain solution require comment. Red cells giving a direct positive reaction to the Coombs test (cord cells, and cells from cases of hæmolytic anæmia) may be classified as Rh-positive even if they are Rh-negative, because the addition of papain (or albumin or serum) can cause clumping of the sensitized cells. There is also the slight danger of $Rh_o(D^u)$ variant pregnant women or recipients being classified as Rh-positive, and possibly immunized to the Rh_o(D) factor, although, in testing, such variants usually give a characteristically weaker type of reaction. An example of Rh_o(D) immunization in an $Rh_o(D^u)$ variant woman has recently been described by Simmons and Krieger (1960).

Summary.

A method for the preparation of an activated papain solution of pH 2·8 to 3·1 has been described. The solution is stable at 5° C. for about 30 days.

Serum-papain mixtures prepared for Rh testing have remained active at 5° C. for periods up to 30 days.

Three methods for the use of low pH activated papain are presented for Rh testing with incomplete anti-Rh sera, and for antibody detection by single-stage and two-stage slide techniques.

In routine blood-bank practice, the methods described have been successfully used in parallel with conventional methods for over twelve months. In blood compatibility testing, papain techniques may be used only to supplement, or precede as a rapid screening test, present methods of cross-matching.

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REFERENCES.

GOLDSMITH, K. (1955), "Papain-Treated Red Cells in the Detection of Incomplete Antibodies", *Lancet*, 1: 76.

GREENWALT, T. J. (1959), Proceedings of the American Association of Blood Banks, *Vox. Sang (Basel)*, 4 (N.S.): 61.

HABER, G., and ROSENFIELD, R. E. (1957), "Ficin Treated Red Cells for Hemagglutination Studies", *P. H. Andresen, Festskrift, Munksgaard, Copenhagen*: 45.

HEKKER, A. C., KLOMP-MAGNEE, W., KRIJNEN, H. W., and VAN LOGHEM, J. J. (1957), "A Papain Slide Test for Rh Mass Typing", *Vox. Sang. (Basel)*, 2 (N.S.): 128.

KUHNS, W. J., and BAILEY, A. (1950), "Use of Red Cells Modified by Papain for Detection of Rh Antibodies", *Amer. J. clin. Path.*, 20: 1067.

LEWIS, A. J. (1957), "Papain, Ficin and Bromelain in the Detection of Incomplete Rhesus Antibodies", *Brit. J. Hæmat.*, 3: 332.

LÖW, B. (1955), "A Practical Method Using Papain and Incomplete Rh-Antibodies in Routine Rh Blood-Grouping", *Vox. Sang. (Basel)*, 5 (Old Series): 94.

MORTON, J. A., and PICKLES, M. M. (1947), "Use of Trypsin in the Detection of Incomplete Anti-Rh Antibodies", *Nature*, 159: 779.

PICKLES, M. M. (1946), "Effect of Cholera Filtrate on Red Cells as Demonstrated by Incomplete Rh Antibodies", *Nature*, 158: 880.

RACE, R. R., and SANGER, R. (1958), "Blood Groups in Man", Blackwell, Oxford.

SIMMONS, R. T., and GRAYDON, J. J. (1945), "Blood Groups, Subgroups, M, N Types and Rh Subgroups in Filipinos", MED. J. AUST., 2: 325.

SIMMONS, R. T., and KRIEGER, V. I. (1960), "Anti-Rho(D) Antibodies Produced by Iso-Immunization in an Rh-Positive Mother of the Unusual Genotype $R^{r}r(CD^{w}e/CdE)$", MED. J. AUST., 1: 1021.

STERN, K., BUSCH, S., and BUXNITSKY, A. (1957), "A Cross-Matching Test Using Activated Papain", *Amer. J. clin. Path.*, 27: 707.

STRATTON, F. (1953), "A Slide Test for the Detection of Rh Antibodies Using Papain Treated Red Cells", *Vox. Sang. (Basel)*, 3 (Old Series): 43.

UNGER, L. J. (1951), "A Method for Detecting Rh_o Antibodies in Extremely Low Titer", *J. Lab. clin. Med.*, 37: 825.

VOGT, E., and HEISTÖ, H. (1953), "A Comparative Evaluation of 8 Different Methods of Detecting Incomplete Rh Antibodies", *Acta path. microbiol. scand.*, 33: 285.

WIENER, A. S., and KATZ, L. (1951), "Studies on the Use of Enzyme-Treated Red Cells in Tests for Rh Sensitization", *J. Immunol.*, 66: 51.

TRIAL OF "ORASECRON" AS A PREGNANCY TEST.

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PATIENTS who reported with a history of amenorrhœa of five to eight weeks' duration were instructed to present a specimen of urine for a pregnancy test (usually a toad test), and then to take five tablets of "Orasecron" (one tablet every four hours) on two consecutive days. The patients were reviewed one week later. A total of 66 patients were investigated.

Results.

Two patients with known primary amenorrhœa were given "Orasecron" on three occasions at weekly intervals without preliminary priming of the endometrium. One patient reported no bleeding; the other experienced "spotting" for one day, on the eighth day after the third course of tablets.

Two other patients were showing signs (blood loss per vaginam) of threatened abortion at the time of testing. In one, these signs subsided within two days, although the patient gave a history of previous abortions. The toad test gave a positive result and the pregnancy proceeded to term. The other patient had an abortion during the trial, and histological examination showed an early precursor of hydatidiform mole.

The results from the remaining 62 patients will be discussed in relation to the reaction to "Orasecron" and then corrected against the toad pregnancy test.

This series falls into three groups: Group I, no bleeding; Group II, bleeding; Group III, only spotting or slight brown staining.

Group I.

Group I consisted of 36 patients who had no bleeding. In 27, the amenorrhœa and positive response to the toad test were confirmed by the continuation of the pregnancy. In five patients, the amenorrhœa continued; but the toad test, which was performed early (after five to six weeks of amenorrhœa), gave a negative result. The patients were ultimately proved to be pregnant, and the result of the single toad test was incorrect. Table I illustrates two of these cases.

Four patients were subsequently found not to be pregnant; this confirmed their negative response to the toad test, and the result of the "Orasecron" test was fallacious.

TABLE I.

Duration of Amenorrhœa.	Test and Result.		
	"Orasecron."	Toad.	Rat.
First case:			
6 weeks	Positive.	Negative.	—
7 weeks	—	Negative.	Positive.
8 weeks	—	Positive.	—
Second case:			
5 weeks	Positive.	Negative.	—
8 weeks	Patient was clinically pregnant.		

Group II.

In Group II there were 21 patients; all experienced bleeding similar to that of a menstrual period within two to seven days. The results of the toad test and the "Orasecron" test were complementary in the cases of this group.

Group III.

Group III comprised five cases in which only "spotting" or slight brown staining occurred. In these cases the signs were those seen in early threatened abortion. Three of these patients gave a positive response to the toad test and were subsequently proven to be pregnant; the other two, who responded negatively to the toad test, were proved later not to be pregnant.

Discussion.

From the foregoing, it is shown that in amenorrhœa of five to six weeks' duration the result of the toad test was incorrect in five instances and that of the "Orasecron" test incorrect in four instances. In Group III the toad test produced a correct result, but the result of the "Orasecron" test was too difficult to evaluate.

Conclusion.

It would appear that the "Orasecron" test is almost as reliable as a single toad test. It seems that "Orasecron" has no harmful effect on pregnancy (many patients treated had a history of previous abortion), and because of its ethisterone content may even be beneficial in a case of threatened abortion.

Acknowledgements.

I wish to thank Dr. N. A. Beischer and Dr. G. O. Smith, of the Royal Women's Hospital, Melbourne, for their assistance in the selection of cases and histories, and British Schering Ltd. for the supplies of "Orasecron".

AN APPARATUS TO AID IN THE TREATMENT OF THE FRACTURED RADIAL AND ULNAR SHAFTS.

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THE difficulties of closed reduction of the fractured radial and ulnar shafts, and the application of a good plaster cast while maintaining the reduction, must be appreciated by all who have attempted this procedure. Some of these difficulties arise from the use of the conventional method of Böhler, in which traction is exerted on a horizontal forearm against a fixed webbing sling above the elbow. This method has the disadvantages that an assistant is required either to maintain the traction or to apply the plaster, that the counter-traction sling prevents the application of a good plaster cast, and that gravity tends to produce angulation at the fracture site.

The vertical method advocated by Charnley (1957) enables the reduction and plaster application to be performed by one person, with gravity aiding correct alignment.

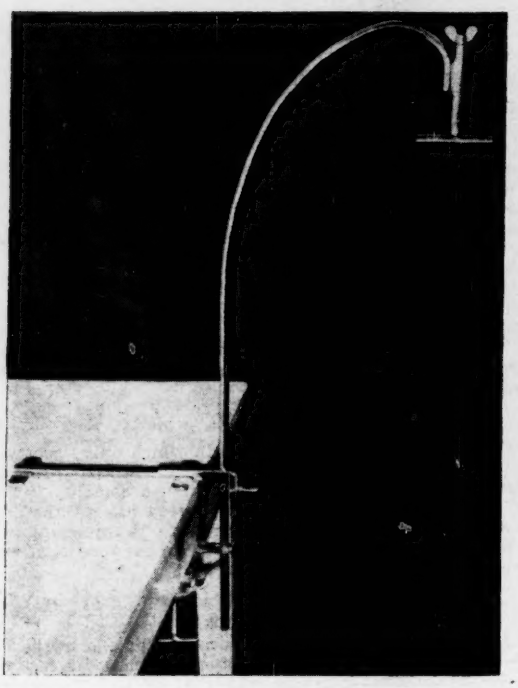

FIGURE I.
The apparatus attached to the plaster table.

We have a simple apparatus in use in the Casualty Department of the Royal Adelaide Hospital, to enable the vertical method mentioned above to be employed for these fractures. This has considerably eased the difficulties associated with them. It consists of a clamp, applied to the plaster table, supporting a vertical rod, adjustable for height, curved over at its upper extremity, to throw its end out about 14 inches from the table edge. At this upper end is supported a short horizontal cross-bar, to which the fingers are strapped with a one-inch strip of zinc oxide adhesive plaster. This cross-bar can be fixed by means of a wing nut so that the hand and forearm are in any desired position of pronation or supination.

The patient lies on his back on the plaster table, with the axilla of the affected arm level with the table edge. The fingers are strapped over the cross-bar, with the vertical support between the middle and ring fingers. The thumb is left free so that plaster may be applied to the web of the thumb and index finger. The support is then adjusted so that the elbow is at right angles, and the forearm is in the desired position of pronation or supination.

Quite powerful traction may be applied to the forearm by pressing downwards on the upper part of the arm close to the elbow with one hand, while manipulating the fracture with the other hand. If it is desired to use both hands for manipulation during reduction, traction may be applied from the operator's foot by means of a looped cord hanging from a webbing sling over the upper part of the arm just above the elbow of the patient. When a stable reduction is obtained, the limb is hanging in position for the application of plaster, and X-ray pictures may be taken before or after the plaster is applied with minimum possibility of redisplacement. The support can also be used during open reduction or other operations on the forearm.

FIGURE II.
The apparatus in use.

The apparatus has been used in over thirty cases of fractured radius and ulna since its introduction. Most of these fractures have been reduced under local anæsthesia, by the use of a regional block of the upper limb nerves in the arm at the level of the pectoralis major insertion. This method is very suited to casualty work, being simple and free of major complications, and giving excellent relaxation for fracture reduction. A paper is in preparation which describes this method and its results in over 180 cases.

Reference.

CHARNLEY, J. (1957), "The Closed Treatment of Common Fractures", 2nd Edition: 100.

Reports of Cases.

A CASE OF IDIOPATHIC HYPOPARATHYROIDISM PRESENTING AS IDIOPATHIC EPILEPSY.

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IN recent years, certain syndromes of hypoparathyroidism have become apparent which are of idiopathic origin. Drake (1939) defined the criteria for diagnosis of idiopathic hypoparathyroidism as follows: (i) a low serum calcium level; (ii) a high serum inorganic phosphorus level; (iii) normal radiological appearance of the skeleton; (iv) the absence of renal insufficiency; (v) chronic tetany; (vi) no history of any operation involving the parathyroid. The raised serum inorganic phosphorus level and normal radiological appearances in the bones differentiate infantile rickets and osteomalacia as causes of tetany. Malabsorption syndromes, such as steatorrhœa, must also be excluded as the basis of hypocalcæmia in these cases.

The case to be reported is one which, by virtue of physical characteristics and biochemical findings, has been diagnosed as idiopathic hypoparathyroidism.

Clinical Record.

A., an Australian-born female, aged 17 years, was referred by Dr. Morris Davis to the Alfred Hospital on February 23, 1959, for endocrinological investigation, in view of the history of epilepsy associated with bilateral cataracts. At the age of eight years she had noticed difficulty in reading from the board at school. Her vision progressively deteriorated, and at the time of her admission to hospital she was unable to read even large type. Five years before her admission to hospital, she had had a generalized convulsive seizure, during which she was unconscious for 20 minutes. She was referred to the Neurology Department at the Alfred Hospital for investigation. General physical examination showed no abnormality, and an X-ray film of the skull and an electroencephalogram were normal. A diagnosis of idiopathic epilepsy was made, and she was given "Dilantin" (100 mg. three times a day) and phenobarbitone (30 mg. twice a day). Since that time she has had three similar episodes of convulsions.

Two years before her admission to hospital, intermittent tingling of both hands appeared on a number of occasions, and there was one episode of carpo-pedal spasm.

The patient had enjoyed good health apart from the symptoms noted above. Her menstrual periods had commenced at the age of 13 years, with a 28 day cycle. She had been delivered normally after a normal pregnancy, and had passed her milestones at normal ages. Her first dentition was normal, but a number of teeth in her second dentition had not erupted. She had not had any dental extractions. The patient was the youngest of four daughters, but had always been of different configuration from them, in that she had a round face and she was shorter and more obese. Her father was 5 ft. 6 in. in height, her mother 5 ft. 4 in., and her three sisters 5 ft. 5 in., and all had weights ranging from nine to ten stone (57 to 63 kilograms). There was no family history of epilepsy, cataracts, round face, congenital malformations or renal disease.

On examination, the patient was seen to be a short, rather obese adolescent with a round face and a short, thick neck (Figure I). The following measurements were taken: height, 60 in.; span, 62 in.; pubis to floor, 32 in.; pubis to vertex, 28 in.; skull circumference, 22·5 in.; weight, 129 lb. Her blood pressure was 140/100 mm. of mercury. Ophthalmological examination revealed bilateral lamellar cataracts involving the periphery of the lenses, which progressed to central lens involvement while the patient was under observation. Examination of her mouth revealed that the canines, second bicuspids and second and third molars of the upper jaw, and the first and second bicuspids and second and third molars of the lower jaw had not erupted. The teeth were widely spaced (Figure II). Apart from the presence of Chvostek's sign, general examination revealed no abnormality. Trousseau's sign was consistently absent. The hands and feet were of normal size and proportion.

FIGURE I.

Female patient, aged 17 years, with idiopathic hypoparathyroidism. Note the round face and short, thick-set build.

A number of investigations were undertaken. The serum calcium levels were persistently low, ranging from 2·8 to 4·3 mEq/l., and the serum phosphorus[1] levels persistently high, ranging from 4·4 to 5·2 mEq/l. The serum alkaline phosphatase level was 17 King-Armstrong units. The response to the Sulkowitch test was negative. The values for other plasma electrolytes were normal — namely: sodium, 143 mEq/l.; potassium, 4·3 mEq/l.; chloride, 101 mEq/l.; bicarbonate, 27 mEq/l.; protein, 18 mEq/l.; urea, 25 mg. per 100 ml. The only abnormality in the electrocardiogram was a *QTc* interval of 0·50 second, consistent with hypocalcæmia. X-ray films of the skull showed no intracranial calcification. However, films of the maxilla showed the canines and second bicuspids to be unerupted.

[1] By serum phosphorus, the serum inorganic phosphorus level is implied.

Only one unerupted molar was present on each side, and there were no erupted molars. The first and second bicuspids in the mandible were unerupted, and again, the only molar teeth present were one unerupted molar on each side (Figure III). The X-ray film of the chest was normal. Films of the forearms and hands revealed slight decalcification of the bones of both upper limbs as compared with the corresponding bones of a normal control of the same age and sex. The relative sizes of these bones were normal. X-ray examination of the renal tract showed a normal intravenous pyelogram, ureterogram and cystogram. A glucose tolerance test produced a normal curve. Examination of fæcal fat revealed 2·6 grammes of fat per 100 grammes of fæces. The basal metabolic rate was normal. No auto-immune antibodies were demonstrated to liver, kidney or thyroid extracts. The electroencephalo-

Figure II.

Photograph of the mouth in a case of idiopathic hypoparathyroidism, showing wide spacing between the teeth and deficient development of the second dentition. Note absence of molars, not due to extraction—see Figure III.

gram showed slightly more activity than was normal for the patient's age. The Ellsworth-Howard test resulted in almost a threefold increase in the urinary excretion of phosphate. In a control there was a twofold increase in phosphate excretion (Table I).

After the Ellsworth-Howard test had been completed, therapy was commenced on May 18, with dihydrotachysterol ("AT 10"), in a dosage of one capsule (0·625 mg.) three times a day with calcium lactate supplements. This had no effect on the serum calcium and serum phosphorus levels. On June 6 the dosage of "AT 10" was increased to two capsules three times a day, but again without effect. On July 6 the dosage of "AT 10" was increased to 20 capsules per day, but one month later the serum calcium level remained low at 3·1 mEq/l. and the serum phosphorus level high (4·0 mEq/l.). It was therefore decided to replace "AT 10" with vitamin D, 250,000 units a day. After two weeks the biochemical levels reverted to normal, as the serum calcium level rose to 5·1 mEq/l. and the serum phosphorus level fell to 2·5 mEq/l.

After six weeks, during which period the serum levels remained normal, a right extracapsular cataract extraction was performed by Dr. J. B. Foster.

Discussion.

On clinical grounds, the association of epilepsy, tetany, dental dysplasia and bilateral cataracts in a young girl of short stature, in whom Chvostek's sign was present, suggested a possible hypoparathyroid state. The diagnosis of idiopathic hypoparathyroidism was confirmed by the low serum calcium and the high serum phosphorus levels in the presence of normal renal function, and by the absence of steatorrhœa as indicated by normal fæcal fat content and the normal response to the glucose tolerance test.

Albright (1942) reported three patients who displayed features consistent with the criteria for idiopathic hypoparathyroidism, but who also had other distinctive findings. These patients had a bodily habitus characterized by a round face and thick-set figure, with brachydactyly especially affecting the metacarpal and metatarsal bones, which were shortened because of early epiphyseal closure. Biopsy of the parathyroid tissue in these patients revealed evidence of hyperplasia in contrast to the pathology of idiopathic hypoparathyroidism, in which fat cells are found in a functionless gland. The condition was termed "pseudohypoparathyroidism", which, it was postulated, was due to a lack of end-organ response, with an inability of the renal tubules to respond to circulating parathyroid hormone.

Ellsworth and Howard (1934) described a test in which fasting levels of calcium and inorganic phosphorus in the serum and urine were compared with levels after the intravenous administration of parathyroid hormone. In a euparathyroid individual there is usually a fivefold to sixfold increase in phosphate diuresis with a fall in serum inorganic phosphorus levels. In idiopathic hypo-

Figure III.

X-ray picture of mandible in a case of idiopathic hypothyroidism, showing one unerupted molar tooth and agenesis of the other two molar teeth.

parathyroidism there is a tenfold or greater increase in phosphate diuresis, said to indicate the absence of circulating parathyroid hormone prior to the test. Patients with pseudohypoparathyroidism have, at the most, a twofold increase in phosphate diuresis, and this diminished response has been considered to be an added criterion for the diagnosis of the condition.

Albright (1952) described a case which differed from pseudohypoparathyroidism only in that the serum calcium and serum phosphorus levels were normal. He called the syndrome "pseudopseudohypoparathyroidism". It has been suggested that the abnormalities found in this condition and in pseudohypoparathyroidism are due to a number of genetic factors which may operate independently.

The possibility of pseudohypoparathyroidism in the present case was considered, as the facial features and the body build described above are more commonly seen in that condition. However, the absence of brachydactyly and soft-tissue calcification were important features against such a diagnosis.

An Ellsworth-Howard test was performed, but its result was equivocal. The phosphate diuresis in this patient represented a threefold increase in phosphate excretion as compared with a twofold increase in the control. This could be held to indicate that the parathyroid hormone used in the test was potent, but of low activity. However, it is known that there is a diurnal variation in the phosphate excretion of normal people, and it is not easy to assess the response in this patient.

Albright and other workers have commented on the difficulty in obtaining potent parathyroid extracts, and on the unreliability of the Ellsworth-Howard test because of this. This is due to the fact that parathyroid hormone has two actions—one on the renal tubules, resulting in phosphate diuresis, and the other on bone, resulting in resorption of calcium. The latter is used as the basis for assaying commercial preparations of the hormone so that the potency of the effect on the renal tubules can vary considerably with each batch that is manufactured.

It would seem unwise to place reliance on the Ellsworth-Howard test as the means of distinguishing idiopathic hypoparathyroidism from pseudohypoparathyroidism. McGregor and Whitehead (1954), in their review of

TABLE I.

Ellsworth-Howard Test, Showing the Hourly Excretion of Phosphorus in the Urine for Three Hours Before and Four Hours After the Intravenous Injection of 200 Units of Parathyroid Hormone.

Time.	Patient.	Control.
First hour	0·50 mEq	1·19 mEq
Second hour ..	0·70 mEq	Specimen mislaid
Third hour	0·90 mEq	1·35 mEq
	200 units of parathyroid injected intravenously	
Fourth hour ..	1·54 mEq	2·25 mEq
Fifth hour	2·35 mEq	2·25 mEq
Sixth hour ..	1·4 mEq	1·49 mEq
Seventh hour ..	1·4 mEq	1·49 mEq

pseudohypoparathyroidism, point out that normal people may not respond to parathyroid hormone extract. They advocate that the criteria for the diagnosis of pseudohypoparathyroidism requires the presence of chronic tetany, together with brachydactyly and the radiological osseous changes in the hands and feet, or with subcutaneous calcification or bone formation.

The dental defects occur frequently in both idiopathic hypoparathyroidism and pseudohypoparathyroidism. Common abnormalities include defects in enamel and root formation and hypoplasia of the teeth. Failure of teeth to erupt in the second dentition is common. However, absence of teeth would seem to be an unusual finding.

The presence of decalcification in the skeleton in cases of hypoparathyroidism was noted by Albright (1956). Decreased calcification of osteoid tissue would seem to be linked with the low concentration of calcium at the bone surface, but its exact mechanism is unknown.

All types of hypoparathyroidism may cause one or more of the following symptoms: tetany or other hypocalcæmic symptoms, such as muscle cramps, paræsthesiæ, laryngeal spasms and stridor; convulsions; mental changes, such as psychoses, memory loss or mental retardation; and cataracts. X-ray examination of the skull may reveal areas of calcification in the basal ganglia, choroid plexus, cerebellum or falx cerebri. However, soft-tissue calcification has been more common in pseudohypoparathyroidism and may even lead to subcutaneous bone formation.

Features in the case under discussion which demand attention are the formation of cataracts and the presence of epilepsy, and the following remarks would be applicable to all types of hypoparathyroidism.

The earliest symptom in this case was progressive loss of vision, due to the gradual formation of cataracts. These were characteristic of the type seen in hypoparathyroid states, in that they were bilateral lamellar cataracts involving the subcapsular areas of the cortex of the lens, and they commenced in the periphery of the lens. If hypoparathyroidism is discovered prior to changes in the lens, cataracts can be prevented. For early diagnosis examination with the slit lamp is essential. Serum calcium and phosphorus levels must be maintained at normal figures before cataract extraction can be undertaken. It would seem wise to make serum calcium estimations on children who present with cataracts.

The real basis of the epilepsy in this patient was considered to be hypoparathyroidism, which had been previously overlooked. This has been so in cases reported elsewhere (Simpson, 1952; Bronsky, 1958). One of the difficulties has been that convulsions have preceded other symptoms or signs of tetany by an interval of years. A rather disturbing association of hypoparathyroidism is the development of papillœdema in some cases, and on occasions this has resulted in the misdiagnosis of cerebral tumour. The papillœdema usually regresses after restoration of the serum calcium level to normal, but it has persisted in one proven case (Steinberg, 1952). It would seem reasonable to include a serum calcium estimation as a routine investigation in all cases of idiopathic epilepsy presenting in childhood, as this is a treatable cause for epilepsy. The electroencephalogram may be abnormal in patients with hypoparathyroidism, but after the serum calcium level has been maintained at a normal figure for some days, the record in many cases will revert to normal.

Treatment.

The aims of treatment in hypoparathyroidism are to maintain the serum calcium and phosphorus levels at normal figures, to prevent further complications such as cataract formation and mental degeneration, and to treat any complications that may be present.

Attacks of tetany respond to 10 ml. of 10% calcium gluconate solution given intravenously.

Therapy may be commenced with "AT10" or vitamin D. In the present case doses of up to 20 capsules of "AT 10" per day produced no result, and only vitamin D was effective. Others report similar experiences. A patient may respond to one agent and not the other, or to both.

Furthermore, the response to a particular drug may vary from time to time. Dosage is a matter of experiment, and the amount should be increased until the serum calcium and phosphorus levels are normal. The mode of action of these two drugs is complex, and involves both the enhancement of the intestinal absorption of calcium and an increased excretion of phosphate by the renal tubules. Vitamin D is a cheaper preparation than "AT 10" and is usually preferred for this reason.

Calcium supplements to the diet, usually in the form of lactate or gluconate, are essential adjuvants to treatment with "AT 10" or vitamin D, as prolonged therapy with these drugs alone may cause decalcification of the skeleton.

Colloidal aluminium hydroxide (100 to 120 ml. per day divided into three doses) is of assistance in lowering the absorption of phosphate in the intestine.

It should be noted that therapy must be continued for the remainder of the patient's life.

In the follow-up investigation of these patients, it is essential to perform frequent calcium and phosphorus estimations. The Sulkowitch test is unreliable (Kerr Grant, 1953). It may give a positive result when hypocalcæmia is present, and a negative result when the serum calcium level is normal. However, it is of value in the detection of the excessive excretion of calcium in the urine, indicating hypercalcæmia with its attendant dangers which may complicate therapy. Clinically, this may be recognized by the symptoms of thirst, anorexia, nausea, vomiting, abdominal pain, constipation, headache, intolerance of noise, photophobia, drowsiness and coma (Howard, 1948). It can cause sudden death. Treatment consists in withdrawal of vitamin D and "AT 10", and of any calcium supplements in the diet (Mowbray, 1954).

Summary.

A case of idiopathic hypoparathyroidism is presented. Essential features were tetany, epilepsy, diminished vision due to cataracts, and dental dysplasia, in the presence of a low serum calcium level and a high serum phosphorus level. A short, thick-set stature and a round face were associated findings.

The method of establishing the diagnosis is described. Therapy with vitamin D caused a reversion of serum

calcium and phosphorus levels to normal. There was no response to dihydrotachysterol ("AT 10").

The importance of performing serum calcium estimations in cases presenting with epilepsy or with cataracts in childhood is emphasized.

Acknowledgements.

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References.

ALBRIGHT, F., BURNETT, C. H., SMITH, P. H., and PARSON, W. (1942), "Pseudo-Hypoparathyroidism. An Example of Seabright-Bantam Syndrome. Report of Three Cases", *Endocrinology*, 30: 922.

ALBRIGHT, F., FORBES, A. P., and HENNEMAN, H. (1952), "Pseudo-Pseudohypoparathyroidism", *Trans. Ass. Amer. Phycns*, 65: 337.

ALBRIGHT, F. (1956), "Hypoparathyroidism as a Cause of Osteomalacia", *J. clin. Endocr.*, 16: 419.

BRONSKY, D., KUSHNER, D. S., DUBIN, A., and SNAPPER, I. (1958), "Idiopathic Hypoparathyroidism and Pseudohypoparathyroidism: Case Reports and Review of the Literature", *Medicine*, 37: 317.

DE MOWBRAY, R. R., SMITH, S. H. L., and SYMONDS, W. J. C. (1954), "Hypoparathyroidism and Pseudohypoparathyroidism", *Brit. med. J.*, 1: 903.

DRAKE, T. G., ALBRIGHT, F., BAUER, W., and CASTLEMAN, B. (1939), "Chronic Idiopathic Hypoparathyroidism; Report of Six Cases with Autopsy Findings in One", *Ann. intern. Med.*, 12: 1751.

ELLSWORTH, R., and HOWARD, J. E. (1934), "Studies on the Physiology of the Parathyroid Glands VII. Some Responses of Normal Human Kidneys and Blood to Intravenous Parathyroid Extract", *Bull. Johns Hopk. Hosp.*, 55: 296.

KERR GRANT, D. (1953), "Papilloedema and Fits in Hypoparathyroidism", *Quart. J. Med.*, 86: 243.

HOWARD, J. E., and MEYER, R. J. (1948), "Intoxication with Vitamin D", *J. clin. Endocr.*, 8: 895.

MACGREGOR, M. E., and WHITEHEAD, T. P. (1954), "Pseudohypoparathyroidism", *Arch. Dis. Childh.*, 29: 398.

SIMPSON, J. A. (1952), "The Neurological Manifestations of Idiopathic Hypoparathyroidism", *Brain*, 75:76.

STEINBERG, H., and WALDRON, B. R. (1952), "Idiopathic Hypoparathyroidism: An Analysis of Fifty Two Cases, Including the Report of a New Case", *Medicine*, 31: 133.

SEVERE RESPIRATORY INFECTION PRESENTING WITH COMA.

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CASES of respiratory tract infection with the development of staphylococcal septicæmia and death within several days of onset have occurred in most Sydney hospitals during 1959. Four such patients at the Prince Henry Hospital, Sydney, have been women; three of the four were in the late teens and early twenties, and the fourth was aged 55 years. A feature of the severe illness seems to be profound toxæmia and collapse out of proportion to the physical signs in the chest, with a temperature which may be subnormal.

In April and May, 1959, two patients were admitted to this hospital several days apart, one comatose, one stuporose. Considerable difficulty was experienced in arriving at a diagnosis in the first case, which exhibited very unusual features; but by the time the second patient was admitted it was possible, with the knowledge gained, to administer rational treatment without delay.

As other similar cases are likely to be met with elsewhere in the future, it is thought that early recognition of the clinical pattern could be life-saving.

Case I.

Clinical Record.

A girl, aged 16 years, was sent home from work at midday with headache, nausea and vomiting. For some six months previously she had felt tired and listless and been in indifferent health. During the night she was restless, and got out of bed several times to vomit. At six o'clock the following morning the family noticed that she was still very restless and noisy; presumably she was delirious at this time. At eight o'clock she could not be roused. No fits had been observed, but she was grimacing frequently and there was twitching of the alæ nasi. She was examined by her doctor, who stated that she was cold, breathing regularly and responding to painful stimuli only. The pupils were dilated and responded to light. There was marked rigidity of the limbs, all deep reflexes were markedly hyperactive and there was a Babinski response on the right side. At midday her doctor found that she was still unrousable, and arranged her immediate admission to hospital.

At 1.30 p.m., on her arrival at hospital, examination revealed her to be a pale thin girl, deeply unconscious, not responding even to painful stimuli, and obviously gravely ill. The skin was cold, and the temperature 97° F. The pulse was weak, the rate being 110 per minute. The systolic blood pressure was 140 mm. of mercury, the diastolic pressure being unrecordable. Respirations were regular, quiet and of average depth, the rate being 30 per minute. Some impairment of percussion note and diminished air entry were noted at the base of the right lung. The pupils were widely dilated and reacted sluggishly to light. Marked spasm of the masseters was noted, and despite the depth of coma the mouth could not be opened. There was jack-knife rigidity of the arms, and the legs were held rigidly extended with both feet firmly plantar flexed. Babinski responses were present on both sides, the abdominal reflexes were absent and the deep reflexes were exaggerated. There was no neck or spine stiffness. The ear-drums and ocular fundi were normal. There was no sugar or albumin in the urine.

The cause of this puzzling clinical picture was not at all obvious. There was no suggestion of the patient's having taken drugs, and in any case it was difficult to think of any drug capable of producing these effects. Tetanus was excluded on clinical grounds. Cerebral hæmorrhage or some type of encephalitis was felt to be more likely. Accordingly, a small quantity of cerebrospinal fluid was obtained for examination. The pressure was normal and the fluid itself was normal in all respects. X-ray films of the skull and chest were normal. The hæmoglobin value was 6·3 grammes per 100 ml., the erythrocytes being markedly hypochromic. The leucocytes numbered 16,600 per cubic millimetre, 85% being neutrophils which showed toxic granulation and a "shift to the left".

At 7 p.m. breathing was regular and heavy, and the state of consciousness was unaltered; but now the arms were held rigidly extended at the sides and the plantar responses were flexor in type. A gastric tube was passed, and the buffered aspirate was injected into mice, which suffered no subsequent ill effects. The temperature was normal.

At 10 p.m., the temperature was rising and the lungs were becoming congested. Penicillin was given in large doses.

Four hours later the temperature was 104° F. and respiration was rapid, the rate being 50 per minute. The limbs were only slightly hypertonic, although tendon reflexes were still exaggerated. The plantar responses were normal. The pulse was weaker, the rate being 160 per minute, and the systolic blood pressure was 110 mm.

of mercury. A mechanical sucker was needed to aspirate frothy yellow fluid from the pharynx.

By nine o'clock on the morning after the patient's admission to hospital her temperature was 101° F., all trismus and rigidity had passed off and the muscles were quite flaccid. Breathing was shallow, rapid, irregular and diaphragmatic in type.

Despite penicillin therapy and a cautious trial of "Bemegride", she died three hours later.

The duration of the illness from first symptom to unconsciousness was 18 hours, and to death, 48 hours.

Autopsy and Histological Findings.

The body was that of a pale, thin young woman.

There was no free fluid in the pleural cavities. The lungs were œdematous in all areas, and exuded a turbid frothy fluid which was present also in the trachea and main bronchi. The latter appeared otherwise normal. There were some patches of consolidation in the lower lobe of the right lung and in the base of the upper lobe of the right lung. Some petechiæ were present over the pleura of the posterior aspects of both lung bases.

Several petechiæ were present over the epicardium of the posterior wall of the heart, which otherwise appeared normal in all respects.

The liver was uniformly pale and somewhat swollen when sections were prepared, the cut surface pouted from the capsule and was also uniformly pale.

There was congestion of the renal cortices.

The adrenals appeared to be slightly larger than normal, but there was no evidence of hæmorrhage on the cut surface.

The brain was abnormally firm in consistence. No focal lesion was found on macroscopic examination, either in the meninges or in the brain substance.

Microscopic examination of sections of lung tissue showed areas of intense bronchopneumonia, together with congestive changes. The air sacs were filled with pink-staining amorphous exudate.

The liver cells generally were swollen, and the cytoplasm stained poorly. The sinusoids were compressed except around the central veins, where there was evidence of red-cell congestion.

Examination of sections of the myocardium of the right and left ventricles showed considerable spacing of muscle bundles due to œdema, and toxic myocarditis was present in the left ventricle.

In sections of the kidneys intense congestion with red cells was seen.

No special changes were seen in the adrenals.

The appearances in sections of the pons suggested toxic damage of the neurons, as a large number stained poorly and in many the nuclei could not be seen.

The Purkinje cells stained poorly, and there was slight Bergmann glial reaction.

In other sections of the brain and cord no special changes were seen.

Case II.

Clinical Record.

Six days later a woman, aged 55 years, was admitted to hospital in a restless, confused state. One week previously she had consulted her doctor for a painful stiff neck. Three days later she experienced pains all over the body and limbs, and was vomiting. The next day an "urticarial" rash appeared on the skin of the arms, and the limbs became extremely tender to touch. The pains became so severe, in fact, that a subcutaneous injection of one-sixth of a grain of morphine gave little relief. "Benadryl" by mouth and calcium injections were given. The following evening she lapsed into stupor, with a weak pulse, small pupils and a very dry tongue.

On her admission to hospital at 4 p.m., she was seriously ill, stuporose, talking irrationally, restless and confused. Her skin was cyanotic, cold and clammy. No pulse could be felt at either wrist, and the blood pressure was found to be 55/40 mm. of mercury. The pressure of the sphygmomanometer cuff and the stethoscope caused considerable pain. Her eyes were roving and her face was twitching; the pupils were small and reacted sluggishly to light. She was able to move all limbs, but the muscles were tender. There was no neck stiffness, although stretching of the cervical muscles was painful. The plantar responses were normal on the right side and doubtfully dorsiflexor on the left. The respiratory rate was 18 per minute. Inspiratory crepitations were present at the base of the left lung, and the breath sounds generally were diminished. At this time her temperature was 97° F.

Blood was taken for culture, and immediate resuscitation measures were started. Three bottles of human serum albumin in isotonic saline together with oxytetracycline were given intravenously. Methedrine was administered intramuscularly and by vein, and oxygen was given by the intranasal route. Salty fluids were fed into the stomach by Ryle's tube.

The leucocytes at this time numbered 21,000 per cubic millimetre, 80% being polymorphs which showed toxic changes and a "shift to the left".

Her condition remained unaltered, and eight hours later the blood pressure was still only 50/30 mm. of mercury. However, her temperature had risen to 102° F. and the respiratory rate to 25 per minute. The intravenous administration of oxytetracycline in large doses was continued.

By 6.30 a.m. the next day she responded to painful stimuli only and auricular fibrillation was present. At 9 a.m. she died, 35 hours after the onset of stupor.

The blood culture yielded a pure growth of *Staphylococcus aureus.*

Autopsy and Histological Findings.

At autopsy, the lungs, liver and brain were stated to have presented a somewhat similar picture to those in the first case. The lungs were very œdematous and exuded turbid frothy fluid, but there were no areas of consolidation.

The liver was paler than normal, but not as pale as in the earlier case.

Although the brain was considered to be slightly firmer than normal, it was not as firm as that of the first patient.

Petechiæ were present posteriorly over the pleura of both lung bases, and over the epicardium of the posterior wall of the heart.

The kidneys were small, granular and contracted.

Microscopic examination of sections of the lungs showed emphysema and collapse, with congestion of the alveolar walls. In some portions of the lungs early pneumonitis was present.

The parenchymal cells of the liver were somewhat swollen, and many contained a fine granular yellow pigment.

The liver sinusoids appeared compressed and contained little blood.

Examination of sections of the brain showed slight changes only in the mid-brain, where in the region of the substantia nigra some perivascular cuffing was seen. In the meninges some inflammatory infiltration was present.

The kidneys showed advanced chronic glomerulonephritis, with some areas of chronic interstitial nephritis.

Discussion.

It was unfortunate that blood cultures were not obtained in the first case before the administration of antibiotics. It is quite likely that acute overwhelming septicæmia probably due to *Staph. aureus* was present, and that the organism's portal of entry was the lung. Tissue resistance presumably was impaired by chronic anæmia and malnutrition. It was evident, from histological study of

sections of the pons, that a severe toxic process had affected the neurons, and it may well be that this was the cause of the clinical state resembling decerebrate rigidity. Odd and changing neurological signs appear not infrequently in hepatic failure, and the liver in this case was certainly badly damaged. The absence in the history of any respiratory infection, and the absence of signs such as purpuric spots or splenic enlargement which may occur in septicæmia, made diagnosis extremely difficult. The persistently low temperature was also misleading. A temperature reading from the rectum is always desirable in doubtful cases.

When the second patient arrived, it was thought that, although the prognosis was obviously poor, immediate treatment might avail. In this case the kidneys, to judge from their macroscopic and histological appearance, had a considerably impaired reserve, which undoubtedly jeopardized the outlook. The explosive rapidity with which the organism spread from the lungs is evident from the fact that the local lung reaction had progressed only as far as intense vascular congestion with migration of leucocytes and œdema fluid into the tissue spaces. Partly as a result of this, physical signs in the lungs were not prominent.

It is obvious that other causes of coma must always be considered in the diagnosis, especially as in many cases appropriate treatment can be life-saving. The metabolic disorders causing coma are usually excluded without great difficulty. A serious mistake would be to neglect treating a narcotic poisoning appropriately. In these cases, however, the patient is deeply comatose and flaccid when there is such a degree of collapse present as to cause hypothermia and hypotension.

Leucocytosis with toxic changes and a "shift to the left" of granulocytes help to support a suspected diagnosis of septicæmia.

One helpful point in the diagnosis of Case II was the extreme tissue tenderness, which has been encountered in other patients suffering from septicæmia. This phenomenon is, of course, not confined to septicæmia, but occurs in cases of acute viræmia, and in other conditions which do not enter into this particular differential diagnosis.

In a case in which the diagnosis of overwhelming infection is likely and other causes of collapse have been excluded, it is reasonable to obtain blood for culture immediately and to start intravenous treatment with antibiotics—for instance, the tetracyclines and erythromycin in large doses. These drugs are suggested because of the prevalence in the community at present of *Staph. aureus* which may be penicillin-resistant.

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ACQUIRED AGAMMAGLOBULINÆMIA.

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SINCE Bruton (1952) first described a case of agammaglobulinæmia in a boy, there have been over 100 cases described in the literature. The condition is sufficiently uncommon to warrant a further report.

Clinical Record.

A female patient, aged 26 years, first presented in 1957 with a history of chest pain, cough and fever. Her past history was one of recurrent episodes of pneumonia, the first one at the age of four years and the seventh at the age of 24 years. She had had rubella and morbilli as a child. The family history was irrelevant.

On her admission to hospital, there were signs of consolidation at the apex of the lower lobe of the right lung which cleared well with chemotherapy. Relevant investigations at the time gave the following results. Culture of the sputum yielded no growth of tubercle bacilli; the Mantoux test (1:1000) produced a positive reaction. A blood count showed that the hæmoglobin value was 10·7 grammes per 100 ml., and the leucocytes numbered 3000 per cubic millimetre. Serum electrophoresis gave the following results (all in grammes per 100 ml.): albumin, 2·8; alpha-1 globulin, 0·6; alpha-2 globulin, 1·3; beta globulin, 1·0; gamma globulin, 0·3; total serum protein content, 6·0. A bronchographic examination prior to the patient's discharge from hospital showed no abnormality in the respiratory tract. During her stay in hospital, a double Jansen-Horgan operation was performed for chronic sinusitis, and she was discharged fairly well, but with the cause of her recurrent pneumonia still unelicited. It is of note that at this stage the significance of the low gamma-globulin level was not realized.

She was readmitted to hospital on April 12, 1959, having had two further episodes of chest infection whilst an outpatient, and she was now complaining of pain in the left subscapular region of one week's duration. Examination of the patient revealed no phyical abnormality except that she was rather pale and had diminished breath sounds in the region of the apex of the lower lobe of the left lung. Investigations on this occasion gave the following findings. X-ray examination of the chest revealed an opaque area in the posterior segment of the upper lobe of the right lung and a patch of consolidation in the apex of the lower lobe of the left lung. Bronchoscopic findings were normal. A blood count gave the following results: hæmoglobin value, 10·9 grammes per 100 ml.—normocytic anæmia; leucocyte count, 5000 per cubic millimetre. Microscopic examination of the fæces revealed no abnormality. The patient's blood was of group O, Rh-positive, with anti-A antigen in a titre of 1:4 and anti-B antigen in a titre of 1:2. Sputum culture produced a growth of *Hæmophilus influenzæ*. Bone-marrow biopsy showed normoblastic erythropoiesis and normal myelopoiesis, but no plasma cells were seen. Liver function tests gave normal results. Paper electrophoresis gave the following results (all in grammes per 100 ml.): albumin, 0·4; alpha-1 globulin, 0·4; alpha-2 globulin, 0·6; beta globulin, 0·5; gamma globulin, 0·1; total serum protein content, 6·5.

The serum was examined by moving-boundary electrophoresis in sodium "Veronal" buffer of pH 8·6, ionic strength 0·1. An instrument with an interferometric optical system was used which, with a photoelectric fringe comparator (Curtain, to be published), is capable of detecting a change in protein concentration equivalent to 0·001 gramme per 100 ml. In the gamma region of the pattern, a concentration gradient due to 0·008 gramme of protein per 100 ml. was observed. The usual values for gamma globulin in a normal adult range from 0·9 to 1·1 grammes per 100 ml. Another interesting feature of the pattern was a split alpha-2 globulin. To my knowledge, this has not been reported previously in acquired or congenital agammaglobulinæmia.

To confirm the virtual absence of gamma globulin, the patient's serum was put up against falling dilutions of a highly specific rabbit anti-human gamma globulin in the ring test of Fornet and Muller (1910). No precipitation was obtained. With the highly sensitive tanned sheep-cell technique of McKenna (1957) a low titre was obtained, but this was at the limit of the specificity of the gamma globulin.

Immune tolerance studies likewise gave negative results. One millilitre of the serum was injected intraperitoneally into each of three newborn rabbits (0 to 6 hours old). Three litter-mate controls were injected with 1 ml. of normal human serum. Starting at 56 days, all rabbits were challenged with three weekly injections of 5 ml. of normal serum adsorbed to aluminium hydroxide. The animals injected at birth with normal serum produced no detectable antibodies. The animals injected at birth with the patient's serum produced antibodies only to gamma

globulin. It has been shown (Curtain, 1959) that the immune tolerance system is capable of detecting very fine differences in the antigenic composition of serum proteins, singly or in mixtures.

The patient's children, both girls, showed the following serum electrophoretic pattern (all in grammes per 100 ml.): (i) A, aged five years: albumin, 4·5; alpha-1 globulin, 0·5; alpha-2 globulin, 0·7; beta globulin, 1·0; gamma globulin, 1·1. (ii) B, aged three years: albumin, 4·3; alpha-1 globulin, 0·4; alpha-2 globulin, 0·7; beta globulin, 0·8; gamma globulin, 1·0.

FIGURE I.
Electrophoretic pattern of patient's serum proteins.

During her stay in hospital the patient had two further episodes of pneumonia of sudden onset, which responded quickly to penicillin and streptomycin. Culture of the sputum yielded *H. influenzæ*. It is interesting that during these febrile episodes she showed the usual leucocytosis with the fever, and the sedimentation rate rose concomitantly. She was diagnosed as having agammaglobulinæmia, but it was decided to treat her with long-term chemotherapy rather than with gamma globulin, and on her discharge from hospital she was taking tetracycline is a dosage of 250 mg. twice a day. When last seen in the out-patient clinic she was well.

Discussion.

Three forms of agammaglobulinæmia have been described—namely, the acquired, the congenital and the transitory (Good, 1956). A further subclassification of the acquired form has been suggested (Firkin and Blackburn, 1958), in which primary and secondary types are described. Our patient seems to fall into the primary acquired group, as there was no evidence of myeloma, nephrotic syndrome or reticulosis to account for the lack of gamma globulin. She shows most of the features associated with this condition—namely, recurrent respiratory infections, normal response to some bacterial infections (Mantoux reaction positive), and low but not completely absent level of gamma globulin on paper electrophoresis. In many cases described, splenomegaly and lymphadenopathy have been present (Citron, 1957), but our patient did not have these features. In common with most of the cases described, this patient had no plasma cells in the bone marrow, and this lends further strength to the hypothesis that plasma cells are the precursors of gamma globulin (Good, 1956).

The suggested treatment of this condition is the administration of gamma globulin in a dose of 0·1 gramme per kilogram of body weight at intervals of two weeks (half-life about 14 days); but we have decided to maintain this patient on long-term broad-spectrum chemotherapy and ascertain her response prior to using gamma globulin. Chemotherapy has been used previously with apparently some success (Good *et alii*, 1956; Zinneman *et alii*, 1954).

Summary.

1. A case of acquired agammaglobulinæmia is described.

2. The features conform to most of those shown in previous case reports.

3. Treatment has been by long-term chemotherapy.

Acknowledgements.

I wish to thank Dr. Roderick Andrew for permission to publish this case and for his advice and helpful criticism. I also thank Dr. C. Curtain, of the Baker Medical Research Institute, Alfred Hospital, for the serum examination and immune tolerance studies.

References.

BRUTON, O. C. (1952), "Agammaglobulinæmia", *Pediatrics*, 9 : 722.

FORNET, W., and MULLER, M. (1910), *"Praktische und theoretische Präzititinuntersuchungen II (Mitteilung)"*, *Z. Hyg. Infekt.-Kr.*, 66 : 215.

McKENNA, J. M. (1957), "A Stable Preparation of Antigen Sensitized Erythrocytes", *Proc. Soc. exp. Biol. (N.Y.)*, 95 : 591.

CURTAIN, C. C. (1959), "The Uses of Acquired Immunological Tolerance and Immunological Paralysis in the Study of the Antigenic Relationships of Normal and Abnormal Serum Globulins", *Brit. J. exp. Path.*, 40 : 255.

GOOD, R. A., and MAZZITELLO, W. F. (1956), "Chest Disease in Patients with Agammaglobulinæmia", *Dis. Chest.*, 29 : 9.

FIRKIN, B. G., and BLACKBURN, C. R. B. (1958), "Congenital and Acquired Agammaglobulinæmia; A Report of Four Cases", *Quart. J. Med.*, 27 : 187.

CITRON, K. M. (1957), "Agammaglobulinæmia with Splenomegaly", *Brit. med. J.*, 1 : 1148.

PEARCE, K. M., and PERINPANAYAGAM, M. S. (1957), "Congenital Idiopathic Hypogammaglobulinæmia", *Arch. Dis. Childh.*, 32 : 422.

ZINNEMAN, H. H., HALL, N. H., and HELLER, B. I. (1954), "Acquired Agammaglobulinæmia; Report of Three Cases", *J. Amer. med. Ass.*, 156 : 1390.

Reviews.

Diagnosis and Treatment of Menstrual Disorders and Sterility. By S. L. Israel, M.D.; fourth edition; 1959. New York: Paul B. Hoeber Inc. 9¼" × 6", pp. 678, with illustrations. Price: $15.00.

THIS book is now in its fourth edition. It has been completely rewritten by Dr. S. Leon Israel, and three new chapters have been added, one on the role of androgens and the others on the thyroid gland and the adrenal cortex in menstrual disorders.

This large volume has always been held in great esteem by gynæcologists, and the new edition has maintained the standard. As its title indicates, there is a marked slant on associated sterility problems. Perhaps the size of the book limits it to any but specialists; but an interested general practitioner would find its valuable contents easy to follow, and any item of desired information may readily be obtained from an adequate index. At no time are scientific considerations allowed to overcloud their practical clinical applications. A particularly good point is the excellence of the reference tables. Many of the photomicrographs are outstanding in their clarity.

Throughout this book, the use of hormones in gynæcological and sterility practice is constantly reevaluated in the light of present-day laboratory information.

Commencing with the physiology of normal menstruation, including the role of androgens, chapters deal with clinical entities such as dysmenorrhœa, premenstrual tension, migraine, breast hyperplasia, intermenstrual pain and vicarious menstruation. Amenorrhœa is discussed fully under the headings of its causes—from central nervous system, pituitary or primary ovarian derangements, and

of uterine origin. Menorrhagia and metrorrhagia are also classified into appropriate ætiological sections.

The thyroid gland and the adrenal cortex in their relationship to menstrual disorders are discussed by Dr. Normal G. Schneeberg, and these chapters present a summary of our latest knowledge in both theory and clinical usage.

The discussion on sterility occupies nine chapters, and is a résumé of all the most modern work in this field. The fact that the author is president-elect of the International Fertility Association lends special authority to this section.

Another practical contribution is a complete section by a urologist, Charles W. Charny, on the male factor in barren marriages. It is pleasing to see stressed the fact that treatment of a moderately fertile male may raise the combined "fertility index" of the couple.

A very human chapter on puberty in the female could well be read in part by the parents of many an adolescent girl. Its summarized knowledge in the hands of a sympathetic family physician would be invaluable.

This edition is almost a new book and is highly recommended. Its presentation with fine paper and first-class illustrations gives the reader an æsthetic pleasure as he peruses it, even if it is somewhat heavy in the hands. It adequately fills in the gaps left in standard gynæcology textbooks, and most certainly should be acquired by all gynæcologists.

Arterial Embolism in the Limbs: The Clinical Problem and its Anatomical Basis. By A. L. Jacobs, M.A., D.M. (Oxon.), F.R.C.P., with a foreword by C. G. Rob, M.C., M.A., M.Chir. (Cantab.), F.R.C.S.; 1959. Edinburgh and London: E. & S. Livingstone Limited. 9¾" x 6¾", pp. 212, with 37 illustrations. Price: £1 15s. (English).

THIS is an excellent study of all aspects of arterial embolism in the limbs. It is based on the author's detailed clinical observations of 122 embolic episodes in 69 patients, supported by a great deal of complementary investigation and research.

Almost every problem in limb embolism is considered, with special attention to pathogenesis, clinical features, morbid anatomy and prognosis. The text is interspersed with valuable summaries of conclusions, based upon evidence presented in so objective a manner that it is hard to disagree with these conclusions. Pathological and experimental observations are made on the role of consecutive or propagating thrombosis after embolism, together with that of diffuse arterial spasm, for which the author can find little supporting evidence.

The section on treatment is less full and a little disappointing. It is surprising that in this series only 6 of 122 patients with embolism were treated surgically, particularly when the author states that "embolectomy still holds first place in the treatment of embolism in the larger limb arteries". His analysis of the disappointing results of embolectomy from other sources does not give due regard to the difference between groups treated surgically and those in which embolectomy is not performed.

The general production of the book is of an excellent standard. It will find an invaluable place in the growing literature of peripheral vascular disease.

Systemic Lupus Erythematosus. Edited by G. Baehr, M.D., and P. Klemperer, M.D.; 1959. New York, London: Grune & Stratton. 10" x 6¾", pp. 84, with illustrations. Price: $3.75.

IT is well known that physicians of the Mount Sinai Hospital have had a particular interest in systemic lupus erythematosus. The writings of Libman, Sacks and Baehr are widely read, and it was Gross in 1932 who first described the hæmatoxylin-stained bodies which are so characteristic of the disease, and which have more recently been shown to be closely allied to the changes in the L.E. cells. Members of the staff have now produced a monograph on the laboratory and clinical aspects of the disease. The opening chapters on pathology and the pathogenetic significance of the L.E. cell phenomenon are written in considerable detail, and the latter contains excellent accounts of the chemical and immunological aspects of the disease. Chapters on blood changes, clinical features and therapy are more discursive and generalized, but contain excellent bibliographies.

A very interesting section discusses the hospital's experience of 15 cases of systemic lupus erythematosus in childhood. All but one of the patients were females, and in four the onset was before the age of 10 years. It would have been interesting to know whether the disease commenced before the menarche, in view of Dameshek's hypothesis that the high incidence in women is associated with sensitization to reticulo-endothelial elements during menstruation.

The monograph is elegantly produced, with excellent histological illustrations, some in colour; one particularly interesting picture shows serially the development of L.E. bodies in leucocytes after the addition of L.E. serum.

Cholera. By R. Pollitzer; 1959. Geneva: World Health Organization. 9¾" x 6", pp. 1019, with illustrations. Price: £5.

THE year 1817 marked the first of a series of cholera pandemics originating from endemic foci in the Far East. In the ensuing one hundred years there were few areas of the world which had not experienced the ravages of the disease. In the efforts to combat this menace its many facets have been intensively studied. The author of the present book, who has a personal experience of cholera control extending over many years, set out to review and to make a critical compilation of the significant literature, a task which extended over a period of three years. The result is a notable addition to the Monograph series of the World Health Organization.

In this large volume each section is dealt with in chronological order, so that the reader is enabled to trace development of thought and progress in research from the earliest work to present-day concepts. The opening chapters deal with history and world incidence, and after these almost one-third of the book is devoted to bacteriology, immunological problems and bacteriophage investigations.

In addition to chapters on general pathology and morbid anatomy and on clinical features and treatment, procedures for practical laboratory diagnosis are outlined in detail. Also, a complete coverage is given in the section on clinical pathology to fluid and electrolyte disturbances, which are important clinically, and whose correction is the sheet-anchor of treatment.

The sum of present-day knowledge of the natural and human factors operating in the epidemiology of cholera is particularly well presented and evaluated. The author supports the view that the role of human carriers in the spread of the disease is of minor importance.

The concluding section is concerned with prevention and control. Great progress has been made in recent years, largely owing to widespread reforms in sanitation, particularly in the provision of safe water supplies, in the undoubted contribution of mass vaccination and in the almost universal adoption of quarantine regulations. However, the author is careful to point out that cholera will remain a potential threat to countries at present free of the disease until much more is achieved in this field, with the accent on eradication measures directed against the endemic foci in Asia.

This volume, of a standard comparable with Dr. Pollitzer's distinguished monograph on plague published by W.H.O. in 1954, very adequately supplies the need for a modern reference work on cholera, and is essential for all medical libraries.

Recent Studies in Epidemiology. Edited by J. Pemberton, M.D., M.R.C.P., D.P.H., and H. Willard, M.D.; 1958. Oxford: Blackwell Scientific Publications. 8¾" x 5½", pp 220, with many illustrations. Price: 25s. (English).

THIS book consists of the papers presented to a study group on current epidemiological research organized by the International Corresponding Club (Preventive and Social Medicine) which met in Holland in September, 1957. The sessions were attended by representatives of 44 university departments in 20 countries. The contents include a summary of conclusions derived from group discussions of the various subjects.

The constituent papers are arranged to illustrate the epidemiological method, which, in the words of one of the contributors, "is taken to mean that technique of studying the occurrence and course of disease in a population—and all the factors which affect it, including the biological, physical and social environment". The contributions are by experts in their fields, about half originating in Great Britain.

The main sections of the work include the following: "The use of Existing Morbidity and Mortality Records in Epidemiological Research"; "The *ad hoc* Field Survey or Getting Your Own Data"; "The Evaluation of Health Needs and Services Including Applications to Under-Developed Terri-

tories"; "Application of the Epidemiological Method to Problems in Mental Health"; "General Practice as a Field for Epidemiology". For each topic, the illustrative papers are informative and well chosen, and describe how epidemiological methods have been applied in practice by their authors to particular problems and the results obtained.

The subjects of many of the contributions are of special interest, apart from their main function of indicating methods. For instance, Alice M. Stewart, of Oxford, describes her study of the effects of fœtal irradiation, to illustrate the use of existing records; W. R. Doll, of London, deals with his statistical investigations of cancer in nickel workers and leukæmia in patients with ankylosing spondylitis treated by radiation; and T. McKeown, of Birmingham, discusses the investigation of institutional facilities for the care of the mentally sick. A pleasing inclusion is a short paper by W. N. Pickles on epidemiology in country practice, which recalls the memorable visit of this rural master to Australia.

The book will be of value to all who have an interest in epidemiology.

Womanhood. By Margaret Moore White, M.D., F.R.C.S., F.R.C.O.G., with a foreword by Professor W. C. W. Nixon; 1958. London: Delisle Limited. 8¼" × 5¼", pp. 144, with 40 illustrations. Price: 17s. 6d. (English).

THIS small book is an addition to the group of Delisle books dealing with sex education, marriage and the family. The author aims at helping young women, wives and mothers "to understand some of the problems, human and medical, which face them in their daily life". She is well qualified to speak from her own experiences as a doctor, wife and mother.

The book is divided into 12 chapters, each dealing with different aspects of womanhood passing from maturity to the menopause. It covers such topics as menstruation, premarital examination and childless marriage, as well as birth control, pregnancy and childbirth. All subjects are discussed in simple language for the layman, with simple drawings as illustrations of the text. Rarely is the discussion oversimplified, although most adults these days would accept "lower part of the stomach" as the lower part of the abdomen. Menstruation and the menopause are dealt with as normal physiological events, while variations from this norm are discussed.

Most of the information and advice given is excellent, and rarely do we disagree, except for the use of baking soda for indigestion in pregnancy, the use of the douche in pregnancy if a rubber ring is worn, and the restriction on the intake of red meat during pregnancy. Careful editing has resulted in only one spelling mistake — "colustrum" for "colostrum". There is an adequate index at the end of the book. Professor Nixon in the foreword states that "it is the purpose of this book to present facts in a way that will help women to lead happier and healthier lives". The author has certainly achieved her purpose.

An Atlas of Normal Radiographic Anatomy. By Isadore Meschan, M.A., M.D., with the assistance of R. M. F. Farrer-Meschan, M.B., B.S. (Melb.), M.D.; Second Edition; 1959. Philadelphia and London: W. B. Saunders Company. Sydney: W. Ramsay (Surgical) Limited. 10" × 6½", pp. 759, with 1466 on 412 figures. Price: £8.

THIS is the second edition of this work, which has been improved, in some instances, by better illustrations and slightly better arrangement. Possibly the best criticism of this book is in the prefaces:

> Once again it has not been our purpose to present an encyclopedic reference but rather a practical, useful text for medical students, general practitioners, residents, especially in Radiology and X-ray technicians.

Also:

> It has been our purpose to make convenient for the student a single compendium of normal radiographic anatomy which will include: (1) basic morbid anatomy as it is applicable to radiography; (2) the manner in which the routine projections employed in radiography are obtained; (3) a concept of the film so obtained; (4) the anatomic parts best visualized on these views; (5) changes with growth and development; and (6) some of the more common variations of normal.

These postulates have been faithfully carried out.

The chapter on bone is particularly good, in that the concept of "living bone" is well put forward and emphasized. The section of the book dealing with technical factors fully explains posturing of the patient, but neglects any factors as to exposure.

Generally the book is quite comprehensive; it is an extremely good practical book of reference and can be recommended.

Textbook of British Surgery. Edited by Sir Henry Souttar, C.B.E., D.M. (Oxon.), F.R.C.S., and J. S. Goligher, Ch.M. (Edin.), F.R.C.S. (Edin. and Eng.); Volume 4; 1959. London: William Heinemann, Medical Books, Limited. 9¾" × 7", pp. 708, with 405 illustrations. Price: £5 5s. (English).

THE fourth and final volume of this textbook deals with orthopædics, and for this, the editors have had the assistance of Mr. Norman Capener as editor of those parts dealing with this subject.

All aspects of orthopædic surgery are covered by well-known surgeons, from pyogenic infections to amputations and artificial limbs. Excellent chapters appear on the surgery of the hand, the surgery of the hip joint, tumours of bone and orthopædics of the spine, to mention but a few of the aspects covered in this volume.

This volume makes an important fourth to the previous three volumes, and reaches their high standard. It is an excellent textbook for the young surgeon reading for the fellowship of the various Colleges of Surgeons.

Progress in Radiation Therapy. Edited by Franz Buschke, M.D., 1958. New York and London: Grune and Stratton, Incorporated. 9" × 5½", pp. 288, with many illustrations. Price: $9.75.

THERE are 13 contributors to this review of radiation therapy, all known in their respective fields.

The history of radiation therapy and of radiation sources suitable for therapy is dealt with first. Radiobiology in particular relation to biological effectiveness, time-dose relationship and the modification of radiation effect by chemical methods including the oxygen defect, is then discussed. The approach of prolonged fractionation, which has proved advantageous in certain carcinomas, is considered by Baclesse; this is particularly interesting to the radiotherapist, as it suggests that the conclusions of Strandquist are not necessarily always true in clinical practice. The cytohistological appraisal of the radiation response in carcinoma of the cervix, and the investigations of the Grahams and of Glucksman, suggest that a more scientific approach is available for the assignment of cases of carcinoma of the cervix to either surgery or radiation therapy. The review here is useful, and points out the difficulties of the method, considers its validity and concludes that it is, as yet, not suitable for general clinical application.

The treatment of intracranial neoplasms is then dealt with; but this section does not provide anything new beyond the usual textbook consideration of the subject. A section reviewing the radiation tolerance of the central nervous system well collates the literature on the subject.

To the practising radiotherapist, Lederman's chapter on the radiotherapy of non-malignant diseases of the eye deals with the subject very ably and should be read.

It is planned to produce a similar volume every two or three years. If subsequent issues measure up to the standard of this first volume, "Progress in Radiation Therapy" will become necessary reading for specialists in this field.

Proceedings of a Symposium on Immunization in Childhood, Held in The Wellcome Building, London, 4th to 6th May, 1959. 1960. Edinburgh and London: E. & S. Livingstone, Limited. 9¼" × 7¼", pp. 140 with many figures. Price: 17s. 6d.

THIS publication is a useful and up-to-date summary of present opinion on the problems of immunization in childhood. A short account of the first two sessions of the symposium, including the two schedules of immunization procedures adopted, has already been published in the *British Medical Journal* of May 23, 1959. The proceedings of all five sessions are here reported in full, complete with tables and illustrations and a wealth of detailed discussion by the 71 participants and observers who attended the conference.

The first quarter of the 140-page booklet is devoted to the risks of immunization, with special sections on provocation poliomyelitis, hazards of pertussis vaccination and faults in the sterilization of syringes and needles. Poliomyelitis, pertussis, diphtheria and tetanus prophylaxis

are then dealt with separately and in detail. A section on the problem of combined prophylaxis follows, and the final section entitled "Discussion and Adoption of Recommendations" is most stimulating where it reports ideas and opinions not always in agreement. The complete text of the recommendations finally adopted is published in a useful appendix. It is difficult to imagine anyone involved in preventive medicine in one of its most practical forms not finding something of interest here.

Fundamental Techniques of Plastic Surgery and Their Surgical Applications. By Ian A. McGregor, M.B., F.R.C.S. (Eng.), F.R.F.P.S. (Glas.), with a foreword by C. F. W. Illingworth, C.B.E., M.D., Ch.M., F.R.C.S. (Ed.), F.R.F.P.S. (Glas.), Hon. F.A.C.S., Hon. F.R.C.S. (Eng.); 1960. Edinburgh and London: E. & S. Livingstone, Limited. 8¼" × 5½", pp. 252, with many illustrations. Price: £1 10s.

THIS small book (235 pages) sets out to describe the basic principles governing plastic surgical techniques and their practical application for surgeons with no plastic surgical training.

The book is divided into two main sections. The first part describes the principles of wound care and suturing, the Z-plasty procedure, free grafting and flap repair. The second part deals with the application of these principles to specific common instances in general surgery, orthopædic surgery and eye-lid surgery. The author succeeds admirably in what he sets out to achieve. The first 90-odd pages in particular are excellent, and should be read by every practising surgeon. The second section dealing with specific application of plastic surgical principles is also particularly good, and there are numerous extremely useful details of technique. All methods described are sound and well proven. The only reservation we might make is that the use of flap repair is made to look a little too easy, and not enough emphasis is placed on the difficulties and dangers. To use flaps successfully requires considerable experience and cannot be learnt out of books. Loss of a flap is frequently a major disaster.

The index is comprehensive and each chapter has a small useful bibliography. The book is well bound, and the numerous photographs and line drawings are first class. This small volume is wholeheartedly recommended, and no surgeon could fail to benefit from reading it.

Radiation Biology of Vicia Faba in Relation to the General Problem. By John Read, B.Sc., Ph.D.; 1959. Oxford: Blackwell Scientific Publications. 8¾" × 5½", pp. 292, with 74 illustrations and 41 tables. Price: 45s. (English).

DR. READ'S collection of the data concerning the radiobiology of the broad bean will be of uncommon interest to all whose work entails a knowledge of radiation and its effect upon the living cell. It is appropriate that there should be an introduction by Dr. L. H. Gray, whose work runs through the text like a vine. Other notable scientists whose data have been heavily drawn upon to support much of the book's findings are J. M. Thoday, S. Wolff, S. H. Revell, P. C. Koller and B. A. Kihlman. The book sets out to correlate and survey the extensive literature of perhaps the main dozen workers in the field, and Dr. Read, as one of those and one who has had early and continuous association with the radiobiology of *Vicia faba*, is well orientated to do this.

Much of the work is devoted to the changes seen in the bean root after irradiation with alpha rays and X or gamma rays, and the results are compared by chosen effects. These effects are alterations in growth rate, inhibition of mitosis and the appearance of chromosome abnormalities. Following this early section of the book there is an important chapter relating the potency of the particular ionizing radiation to its mean linear energy transfer (LET). On the whole it is concluded that chromosome damage results from the passage of ionizing particles through and close by the chromosomes. A strong case is made for the importance of nuclear damage in the radiation effect. Further chapters deal with the effect of dissolved oxygen, and the influence of cyanide and large gas pressures upon radiosensitivity. There is a comparison of the action of radiomimetics and radiation, and the evidence is sifted to show that cells are most sensitive to damage by X rays and, for example, nitrogen mustard at different phases of the cell cycle. Finally Dr. Read states his philosophy of the *Vicia faba* work, and rightly infers that the direct effects of radiation upon his medium chronicled in this cohesive book are of basic importance to human radiotherapy and carcinogenesis.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Intussusception in Infants and Children", by Mark M. Ravitch, M.D.; 1959. Springfield, Illinois: Charles C. Thomas, and Oxford: Blackwell Scientific Publications Ltd. 11" × 8½", pp. 136. Price: 76s. (English).

"Studies in Radiotherapeutics", by J. S. Mitchell, C.B.E., M.D., F.R.S.; 1960. Oxford: Blackwell Scientific Publications. 9¾" × 7½", pp. 284. Price: 52s. 6d. (English).

"An Introduction to Human Blood Groups", by Fulton Roberts, M.D.; 1960. London: William Heinemann Medical Books Ltd. 7¼" × 4¾", pp. 88. Price: 9s. 6d. net (English).

"Lecture Notes on Ophthalmology", by Patrick D. Trevor-Roper; 1960. Oxford: Blackwell Scientific Publications. 7" × 4¾", pp. 100. Price: 12s. 6d.

"Blood Transfusion: A Guide to the Practice of Transfusion within Hospitals", by George Discombe, M.D., B.Sc. (Lond.); second edition, 1960. London: William Heinemann Medical Books Ltd. 7¼" × 4¾", pp. 64. Price: 6s. net (English).

"Electrocardiographic Techniques: A Manual for Physicians, Nurses and Technicians", by Kurt Schnitzer, M.D.; second edition, 1960. New York and London: Grune and Stratton. 8¾" × 5¾", pp. 126. Price: $4.75.

"Drugs of Choice 1960-1961", edited by Walter Modell, M.D.; 1960. St. Louis: The C. V. Mosby Company. 9¾" × 6½", pp. 960. Price: £7 8s. 6d.

"Symposium on Glaucoma", edited by William B. Clark, M.D., F.A.C.S., assisted by Joe M. Carmichael, M.S.J.; 1959. St. Louis: The C. V. Mosby Company. 9¾" × 6¾", pp. 320. Price: £7 8s. 6d.

"Medical Care of the Adolescent", by J. Roswell Gallagher, M.D., and The Staff Physicians of the Adolescent Unit; 1960. New York: Appleton-Century-Crofts, Inc. 9¼" × 6", pp. 394, with illustrations. Price: $10.00.

"Exposition and Critique of the Conceptions of Eddington Concerning the Philosophy of Physical Science", by Johannes Witt-Hansen; 1958. Copenhagen: G. E. C. Gads Forlag. 9¼" × 6¼", pp. 128. Price not stated.

"The Pædiatric Prescriber", by Pincus Catzel, M.B. (Rand), M.R.C.P. (Edin.), D.C.H., R.C.P. & S. (Eng.), assisted by S. Cohen, M.P.S. (S.A.); 1959. Oxford: Blackwell Scientific Publications. 6¾" × 4", pp. 260. Price: 15s. (English).

"The Diabetic ABC: A Practical Book for Patients and Nurses", by R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.); twelfth edition; 1960. London: H. K. Lewis & Co. Ltd. 8¾" × 5¾", pp. 96. Price: 5s. 6d.

"An Introduction to the Anæsthesia of Laboratory Animals", by Phyllis G. Croft, Ph.D., M.R.C.V.S.; 1960. London: The Universities Federation for Animal Welfare. 8¾" × 5½", pp. 32. Price: 3s. 6d. (English).

"Pædiatric Tutorials: The Newly Born Infant", by Andrew Bogdan; 1959. Sydney: Angus & Robertson, Limited. 7¾" × 3¾", pp. 38. Price: 4s. 6d.

"Notes on Some Improved Measures in the Prevention of Staphylococcal Cross Infection", by R. T. B. Green, C.B.E., M.D., D.Sc.; 1960. 9¾" × 7¼", pp. 12, with 13 illustrations. Price not stated.

"Deafness: A Comprehensive Account of Deafness as it Affects People of all Ages", by J. Chalmers Ballantyne, F.R.C.S., D.L.O.; 1960. London: J. and A. Churchill Ltd. 8" × 5¾", pp. 264, with 71 illustrations. Price: 25s.

"The Psychological Report: Use and Communication of Psychological Findings", by Walter G. Klopfer, Ph.D., and Leopold Bellak, M.D.; 1960. New York and London: Grune and Stratton Inc. 8½" × 5½", pp. 156, with illustrations. Price: $4.50.

"Nutritonal Evaluation of Food Processing", edited by Robert S. Harris and Harry von Loesecke; 1960. New York: John Wiley and Sons Inc. 9" × 5¾", pp. 630, with illustrations. Price: $12.00.

"A Practice of General Anæsthesia for Neurosurgery", by Robert I. W. Ballantine, M.R.C.S., L.R.C.P., D.A., F.F.A.R.C.S., and Ian Jackson, M.R.C.S., L.R.C.P., D.A.; 1960. London: J. and A. Churchill Ltd. 8" × 5", pp. 166, with illustrations. Price: 27s. 6d. (English).

"Hypnotism for Medical and Dental Practitioners", by A. A. Mason, M.B., B.S., with chapters on hypnosis in Dental Surgery and Obstetrics by K. Dawson Watts, F.D.S.R.C.S., and S. D. Perchard, M.D., M.R.C.O.G.; 1960. London; Secker and Warburg. 8½" × 5¾", pp. 224, with illustrations. Price: 49s. 9d.

The Medical Journal of Australia

SATURDAY, AUGUST 6, 1960.

THE CONTROL OF TUBERCULOSIS IN AUSTRALIA.

Since the introduction of the *Tuberculosis Act* in 1948 the Commonwealth Government has spent more than sixty-three million pounds towards the control of tuberculosis. This money has been well spent. There has been a steady and, more recently, a dramatic fall in the annual number of deaths from this disease, and during the last five years fewer new cases of tuberculosis have been reported to the authorities. Several sanatoria have been closed, and in those that remain open there are many empty beds. The amount being paid in tuberculosis allowances is diminishing. The disease is certainly being brought under control.

But where do we go from here? Should we just carry on as we are doing? Has the time arrived when we can relax our efforts a little? Or should we increase our attack? Should we now lift our sights and aim at the elimination of tuberculosis from our midst? The World Health Organization considers that the disease will have been eliminated as a public health problem when "the prevalence of natural reactors to tuberculin among the children aged 14 years has become less than one per cent". So perhaps it would be better to say that we must aim at virtual elimination.

About every ten years there has been a definite advance in the methods available for the control of tuberculosis. Before World War II and during the war years emphasis was placed on the necessity for rest in sanatoria, and until about 1950 one of the problems was the provision of sufficient sanatorium beds. Mass miniature radiography, as used for the examination of the members of our armed forces, paved the way for community-wide surveys in many areas in the post-war years. These surveys led to more extensive case-finding, and the need for more sanatorium beds was increased. They also moved the emphasis from the care of the individual patient to the importance of tuberculosis, an infectious disease, as a public health problem in the community.

The discovery of the three drugs, streptomycin, PAS and INH and the experience of how to use them gained in the 1940's and 1950's have now given hope that we can control this disease, and we can at last hope "virtually to eliminate" it from our midst. That this is a practicable possibility was supported by representatives of the United States Public Health Services and of the National Tuberculosis Association at their Arden House Conference held at the end of 1959. A condensed summary of the discussions is available in the February, 1960, issue of the *Bulletin of the National Tuberculosis Association*, and it should be studied by everyone interested in this subject. The following quotation is important:

> The major recommendation of the Conference is a program for the widespread application of chemotherapy as a public health measure for the elimination of tuberculosis in the United States. Goal—To sterilize that important part of the reservoir of tubercle bacilli that presently exists throughout the country in persons currently suffering from active tuberculous disease, whether presently known or unknown to public health authorities, and in selected persons who previously have had active disease and were inadequately treated.

There were eleven other recommendations from the Conference, mainly dealing with the implementation of this major one. This means that adequate chemotherapy is recognized as a public health control measure. If our aim is eradication of tuberculosis from Australia we must accelerate our case-finding programmes, we must investigate contacts more thoroughly, we have greater need of up-to-date case registers and of notification of every case of tuberculosis, and we should make far greater use of tuberculin skin testing, of B.C.G. vaccination of non-reactors who are living or working at risk, and of mass miniature radiography of selected groups — the high incidence groups and the danger groups. Lastly, we must be sure that the drugs are given in proper dosage "continuously over an adequate period of time" so as "to destroy tubercle bacilli in the human body, render the patients' disease non-communicable to others, and minimize the possibility of reactivation". To achieve this the enthusiastic cooperation of the whole medical services and of the ancillary services will be needed, for although wherever practicable use will be made of hospital and/or sanatorium beds for early treatment, the great bulk of it will be continued on a domiciliary or ambulant basis.

These comments are not intended to reflect adversely on the excellent work that has been done and is being done by the Commonwealth and State Departments of Health and by various non-governmental agencies throughout Australia. Rather are they a call to consolidate and to capitalize on our gains, and to maintain a realistic attitude. There is a growing tendency, both here and abroad, to regard the attack on tuberculosis as "all over bar the shouting". That is far from the truth. The real need is to push on more vigorously than ever if we are not to be defeated by drug-resistant organisms. It has been estimated that unless a new drug is found for the effective treatment of tuberculosis, we have only about ten years in which to drive home our advantage.

A MUNIFICENT GIFT FOR RHEUMATISM RESEARCH.

On July 25, 1960, a Sydney businessman, Mr. F. G. Spurway, presented a cheque for £100,000 to the Australian Rheumatism Council for use in research. No binding conditions were attached to the gift, one of the most notable in the history of medical research in Australia, but it is expected that the income only from investment

of the capital sum will be used and that a substantial proportion of it will be disbursed in New South Wales. The important point, however, is that it will be available for research in this country into the obscure but devastating group of diseases still loosely grouped around the term rheumatism.

These twin aspects of the rheumatic group of diseases—the obscurity of their nature and cause, and the devastation wrought by their capacity to cause pain and crippling—make them a particularly apt and urgent subject for searching investigation. Yet, as the chairman of the Australian Rheumatism Council, Dr. C. G. McDonald, remarked at the time of the presentation of Mr. Spurway's gift, they have been something of a Cinderella in medicine. Why this should be so is hard to say. It is understandable, if regrettable, that clinicians should find the management of these diseases a depressing affair and tend to leave the main responsibility for them to the few who are fortified with an unusual abundance of patience, hope or compassion. It is surprising, however, that more with the spirit of the investigator have not seen here a challenge for research as great as any in medicine. Perhaps the lack of financial endowment has been the discouraging factor.

Be that as it may, Mr. Spurway's truly munificent gift opens up great possibilities, for which we may confidently hope his fellow men will come to be deeply grateful to him. For the Australian Rheumatism Council, a group of doctors and laymen voluntarily banded together to do something practical about the problem of rheumatism, the gift is a source of great encouragement. Ever since it stemmed off from the Empire Rheumatism Council, the Australian Rheumatism Council has met with difficulties almost as crippling and depressing as rheumatism itself. Now a new door is opened, and the Council will be encouraged to renew and extend its efforts. It needs all the support, financial and otherwise, that it can get. We may well hope that Mr. Spurway's example will stimulate others to join the side of the angels in one of medicine's most bitter battles.

Current Comment.

THE INCIDENCE OF SHEEHAN'S SYNDROME.

ONE important excuse for writing about unusual syndromes is that many of them can easily pass unrecognized, to the patient's detriment, if the possibility of their occurrence is overlooked. This is certainly true of hypopituitarism developing after post-partum hæmorrhage and/or shock, a condition often referred to as Sheehan's syndrome, though such cases are in fact a special group of the more general classification of Simmonds' disease.

Not long ago we published an article by B. J. Pascoe and A. E. McGuinness[1] in which they described eight cases of post-partum panhypopituitarism seen at Sydney Hospital in the space of four years. Some of these cases had passed unrecognized for many years, and this is characteristic of the syndrome, one of the principal reasons being that, though failure of lactation and persistent amenorrhœa are the characteristic early symptoms of the disease, the full picture of loss of energy and apathy, genital and breast atrophy, loss of pubic and axillary hair, sterility, symptoms and signs of hypothyroidism, and various degrees of adrenocortical insufficiency may not become evident for years, and may be incomplete in various respects. In a more recent article, N. G. Schneeberg, W. H. Perloff and S. L. Israel[2] discuss the incidence of unsuspected "Sheehan's syndrome". The interest of one of the authors in the subject had been stimulated by a case reported some years previously[3] in which a patient suddenly collapsed and died during an operation for Cæsarean section. In the light of the post-mortem examination, which revealed extensive pituitary necrosis and some degree of adrenal cortical atrophy, it became evident that the patient had suffered from unsuspected chronic hypopituitarism since her previous pregnancy (which had been complicated by massive post-partum hæmorrhage) and that death was due to consequent adrenal insufficiency. The patient's only symptom had been excessive fatigue, though in retrospect there were other features of her history which might have aroused suspicion. In their present communication Schneeberg *et alii* report the results of the study of 35 patients with a history of post-partum hæmorrhage and shock in an effort to determine the incidence of pituitary insufficiency among such persons, and to identify any patients so discovered as potential candidates for shock in the event of their being subjected to severe stress. The patients' histories were studied in detail, and an extensive battery of laboratory tests performed, including a variety of hormone assays. In the event, four cases of previously undiagnosed pituitary insufficiency were discovered. The most severely affected patient had been under treatment for years with a diagnosis of myxœdema with intolerance of thyroid medication, another had symptoms of adrenocortical insufficiency, and the remaining two had relatively minor degrees of hypopituitarism. In all the diagnosis of Sheehan's syndrome was strongly suspected on clinical grounds, but the laboratory studies were needed to confirm the diagnosis and to define the pituitary target organs involved. Only the myxœdematous patient showed the full picture of panhypopituitarism; two showed loss of gonadotropins and partial loss of adrenocorticotropins, and one showed loss of gonadotropins only. In four other patients the results of investigation were classed as equivocal, but the diagnosis of hypopituitarism was considered unlikely. In two, early laboratory studies, carried out during the first few months after the hæmorrhage, were suggestive of hypopituitarism, but subsequent studies showed that all values had returned to normal; this suggests the possibility of transient pituitary depression. Schneeberg *et alii* were surprised at the lack of correlation between the severity and the duration of shock and the subsequent development of pituitary insufficiency. The six patients in their series who had been most gravely ill at the time of their hæmorrhage were all found to be normal from the standpoint of endocrine function when subsequently examined. On the other hand one patient whose complaints were amenorrhœa and sterility, and who was found to be suffering from gonadotropic depression, had sustained only a minimal post-partum hæmorrhage.

Since the 35 patients of Schneeberg *et alii* were not a random sample, the incidence of hypopituitarism among them is not a true measure of its frequency in such cases. Various other authors have made similar estimates, but all are open to the same objection. In New Zealand, R. W. Hornabrook and J. E. Caughey[4] traced 70 patients who had experienced a post-partum hæmorrhage of 30 ounces or more, and found one case of severe hypopituitarism and two of mild degree, but they also noted that 30 of these patients "had minor changes which seemed to indicate a restricted lesion of the pituitary gland with resulting impairment of function of a single end organ". However, as Schneeberg *et alii* point out, their conclusions were based on clinical evaluation only, and there is no mention of laboratory studies in the latter cases. The weakness of Hornabrook and Caughey's

[1] MED. J. AUST., 1959, 2: 635 (October 31).

[2] *J. Amer. med. Ass.*, 1960, 172: 20 (January 2).

[3] *J. Amer. med. Ass.*, 1952, 148: 189 (January 19).

[4] *N.Z. med. J.*, 1954, 53: 210 (June).

figures lies in the fact that they were able to trace less than 50% of the patients who had suffered from severe post-partum hæmorrhage during the period selected for review. Schneeberg *et alii* conclude that though "Sheehan's syndrome" is one of the rarer endocrinopathies, it is more common than is generally supposed, and many cases are still overlooked. Because of the lack of correlation between the amount of blood loss or the profundity of shock and the subsequent appearance of hypopituitarism, they recommend that all survivors of this obstetric complication, however mild, should be kept under surveillance until the possibility of the late development of a mild degree of hypopituitarism has passed. It should be noted that suppression of lactation does not always occur, or may be incomplete; in exceptional cases transitory return of menstruation has been recorded; and there are a few reports of cases in which the patient has become pregnant again. In fact, no one element of the syndrome is entirely constant. Schneeberg *et alii* urge that even in obvious clinical examples of pituitary insufficiency careful laboratory studies should be performed to define more clearly the extent of endocrine damage and to determine the subsequent needs for substitution therapy.

The question of whether there may not be a minor degree of pituitary depression, which may or may not be permanent, in a much larger proportion of patients who have suffered a severe post-partum hæmorrhage appears very uncertain. As has been noted, Hornabrook and Caughey thought that this was so in over 40% of their patients. It is possible that only a therapeutic trial could establish the presumptive diagnosis in such cases.

DENTAL CARIES AND SOIL CONSTITUENTS IN NEW ZEALAND.

IN a publication of the Medical Research Council of New Zealand in 1955 R. E. T. Hewat and D. F. Eastcott reported that a relationship existed between prevalence of caries and certain soil conditions in New Zealand. T. G. Ludwig, W. B. Helay and F. L. Losee[1] have been studying this matter in much greater detail and have presented a preliminary report. One phase of the investigation involves the study of the effect on prevalence of caries of recent saline soils in Napier, Hawkes Bay. In 1931 extensive earthquakes resulted in the uplifting of an area of the country around Napier to heights ranging up to 9 feet in an area 60 miles long and 10 miles or more wide. Five square miles of an extensive salt lagoon adjacent to the city were drained. The reclaimed land has since gone into production and use as a residential area. In order to establish a baseline to judge the effectiveness of fluoridation of the water supply of the neighbouring city of Hastings, during 1954-1955 dental examinations were undertaken of children who had lived all their lives either in Napier or in Hastings. It was found that the Napier children, aged 5 to 8 years, had a considerably lower incidence of caries than the children of equivalent age in Hastings. This was surprising because the two cities differ little in situation and population. The water supply of the two cities comes from the same artesian strata, and analysis showed that the normal mineral composition of the two supplies was similar. Examination of the urine of Napier children made it unlikely that they received extra fluoride from any source. The dental examinations were repeated in 1957, and it was found that the fluoridation of the Hastings water supply, over a period of about two and a half years, had reduced the caries incidence to approximately the same as that in Napier. Children in Palmerston North, about 110 miles from Napier and on similar soil to Hastings, were dentally examined, and the relation between caries prevalence in Napier and Palmerston North in 1957 was closely comparable to that between Napier and Hastings in 1954. Analysis of the soils from Napier and Hastings showed little difference, except that the Hastings soils were acid while the Napier soils were alkaline and contained much more calcium. A large range of vegetables grown on the soils from the two cities was examined for trace elements. In general Napier vegetables contained more molybdenum, aluminium and titanium than Hastings vegetables and less copper, manganese, barium and strontium. Various investigators have suggested that molybdenum is of importance in tooth development. It was found in only one Hastings vegetable, whereas it was present in nearly all Napier vegetables in amounts up to 9·5 p.p.m. This points to a greater availability of molybdenum in the Napier soils due in the main to higher pH. It seems possible that the intake of molybdenum accounts for low figures for the incidence of caries in Napier, and that much more work is needed before the relation between mineral intake and tooth development is cleared up.

[1] *Nature*, 1960, 186: 695 (May 28).

MARSUPIAL MILK.

As every schoolboy knows, marsupial young are born at a very immature stage, make their way to the mother's nipples, and there remain attached until they are ready to move about independently. For this reason it has been thought that the study of marsupial young might help to throw light on some of the problems surrounding the care of the human premature infant. Dr. Ethel Dunham has stated this view in an article published three years ago.[1] She enlisted the aid of R. Gross and A. Bolliger[2] of Sydney in the project, and these workers have now produced a very interesting paper[3] on the composition of the milk of the common brush-tailed possum (*Trichosurus vulpecula*). An adult brush-tailed possum weighs about three to four pounds, but its single young at birth, after a gestation period of about 20 days, weighs less than half a gramme. After entering its mother's pouch, it attaches itself to one of the two nipples, and remains firmly attached for the first six to ten weeks of its life. After this it suckles intermittently, and weaning is not begun till it is five or six months old. By the exercise of considerable ingenuity Gross and Bolliger were able to collect over 50 samples of milk from possums with young of various ages, and analyse them for their content of total solids, protein, fat, lactose, calcium and phosphorus. It was found that in the transitional period (with young 18 to 65 days old) the milk was more dilute than the mature milk (young 88 to 193 days old). In mature milk the composition was comparable with that of the more concentrated milks produced by eutherian mammals (on an average the content of total solids was 24·5%, protein 9·2%, fat 6·1% and lactose 3%). The protein content was initially high, as might be expected from the rapid rate of growth in the pouch, and increased up to the time when the young began to take other food. The total body iron content was satisfactorily maintained by the iron derived from the milk. In this connexion Gross and Bolliger note that during the first three months of life the young is completely enclosed in the pouch and that the excretory products are apparently mainly reabsorbed, either through the lining of the pouch or through the thin skin of the hairless young; it is suggested that this arrangement may serve, *inter alia*, as an iron-conserving device. The carbohydrate fraction is expressed as lactose, but the milk actually contains a considerable amount of free galactose units. Gross and Bolliger suggest that fundamental differences between the milk of marsupials and that of eutherian mammals may reside more in the qualitative than in the quantitative field.

[1] *A.M.A. J. Dis. Child.*, 1957, 94: 372, (October).

[2] In collaboration with J. V. Pascoe, Bolliger had previously published an analysis of the composition of kangaroo milk.

[3] *A.M.A. J. Dis. Child.*, 1959, 98: 768 (December).

Abstracts from Medical Literature.

ORTHOPÆDIC SURGERY.

Accident Services and the Orthopædic Surgeon.

J. C. SCOTT (*J. Bone Jt Surg.*, November, 1959), of Oxford, discusses the claims of the orthopædic surgeon to manage an accident service. Injuries of the locomotor system make up 75% of any unselected group of accidents. It is unsound to distinguish fractures and major soft tissue injuries. The break in a bone is not an essential "open sesame" to the orthopædic department. He discusses the incidence and the types of accident. In 1955 the Royal Society for the Prevention of Accidents noted that in Britain road accidents caused 5526 deaths out of a total of 18,663 deaths due to accident. Domestic accidents were more common than either road or industrial accidents. In any effort to cope with this situation the importance of organization is stressed. A serious accident takes place and there is no time for the patient to decide where he is to go. He is swept into the organization and depends upon it for the standard of his treatment. This organization must be prepared to cope with the simplest fractured phalanx as well as with severe injuries. The author describes the Oxford Accident Service at the Radcliffe Infirmary, which deals with the accidents from a population of 600,000. The orthopædic surgeon accepts responsibility for the organization of the treatment of all injuries, but treats only injuries to the locomotor system, burns and septic fingers. A neurosurgeon is on the staff with a neurosurgical registrar. There are two junior registrars and a senior registrar in the orthopædic section. Injuries that are multiple remain in the department and are cared for by the appropriate specialist. If the injuries do not involve the locomotor system, they are transferred to the appropriate department in the general hospital. The author notes that a reasonable amount of interdepartmental goodwill and cooperation is required. He also warns of the difficulties to be met with in organizing an accident service, and stresses that the orthopædic surgeon must be concerned with more than the nominal control of the service and not leave work to juniors. This was the bugbear of the casualty arrangement for many years.

Three Types of Acute Hæmatogenous Osteomyelitis.

J. TRUETA (*J. Bone Jt Surg.*, November, 1959) discusses acute hæmatogenous osteomyelitis in the light of 202 patients seen since 1944. He notes that in the literature there are three types of acute osteomyelitis, that affecting infants, that affecting children, and the condition in the adult. In infancy and adulthood the condition is more serious to life and destructive to bone and joint than in childhood. The factors influencing the localization of the pathogenic bacteria are considered, and the author recalls Koch's experiments in 1911 in which, after intravenous injection of bacteria, these were located in the metaphyseal veins two hours later. The author suggests that the changing vascular arrangement is the factor which determines the diverse clinical picture of acute osteomyelitis in each group affected. The disease is commonest in childhood, and in this age group has been carefully studied. The capillaries developing from the nutrient vessel turn on themselves when they reach the cartilaginous growth plate. Here they run into large sinusoidal veins which are partly responsible for the hæmopoietic activity of the bone marrow. Here the blood is slow and here is an ideal medium in which organisms may multiply. With infection in these metaphyseal veins there is early œdema, and this expands towards the surface of the bone, across the cortex, where this is thinnest; this causes separation of the periosteum and disruption of vascular connexions between the periosteum and the cortex; the nutrient vessel also becomes blocked by coagulation. This accounts for the development of early new bone under the periosteum and the formation of the involucrum. In the child up to the age of one year these end vessels cross into the forming epiphysis and expand underneath the surface of the joint; this accounts for the more rapid extension of infection and the commonness of joint involvement; there is also profuse involucrum formation, sometimes monstrously large. This bulging new bone is easily palpable but is transient and disappears with the remodelling of growth. True acute osteomyelitis is rare in adults, but when it occurs it spreads rapidly through the whole length of the bone, involving the joint, destroying the cortex and thus leading to pathological fracture in many cases. The periosteum is fibrous and does not strip off, so involucrum is not a feature.

Herniated Lumbar Intervertebral Discs.

F. S. WEBSTER AND D. P. SMILEY (*Amer. J. Surg.*, January, 1960) attempt to evaluate the relative merits and results of surgery with and without bony stabilization in a series of 200 operations for herniated lumbar discs. The follow-up period ranged from two to ten years. Each patient had a complete trial of conservative management without relief prior to operation. A total of 190 myelographic studies were made and, except for seven patients, X-ray changes were well correlated with the pathological findings at operation. One hundred and twenty patients in the series had simple excision of the herniated disc, and in 80 the disc was removed with additional fusion. When all satisfactory results (i.e., all those classed as excellent, good or fair) were considered together, improvement was shown in 94% of cases in both groups, and in 6% the result was poor. Thus it would appear that both procedures give essentially an equal degree of success. However, after a lengthy follow-up period those patients with fusion were superior. Pseudarthrosis through the bone graft was radiologically demonstrated in seven patients. In one of these this occurred at the third lumbar level, where the authors now believe fusion should not be performed because of the risk of pseudarthrosis; in the others it was at the level of the fourth interspace and occurred in two-level fusions. In view of the absence of pseudarthrosis in one-level fusions, it is believed that the more extensive stabilization procedure should not be carried out for lesions in the lumbo-sacral area unless degenerative disc changes are evident at the level above. Although there is a chance of a recurrence of herniation above the level of a single fusion, this is less than the risk of complication after a more extensive fusion. The appearance of narrowing of the disc space radiologically did not appear to be of direct diagnostic significance, as in several cases rupture of the disc occurred at the level above the narrowed space. It was further found that in both those with fusion and without fusion the degree of degeneration as indicated by osteophytic reaction and narrowing of joint space did not reliably predict the outcome of operation.

Infantile Structural Scoliosis.

J. I. P. JAMES, G. C. LLOYD-ROBERTS AND M. F. PILCHER (*J. Bone Jt Surg.*, November, 1959) report the outcome of structural scoliosis of unknown ætiology in 212 infants, all less than three years old. These attended the scoliosis clinic at the Royal National Orthopædic Hospital in London. It was apparent that there were two types of infant structural scoliosis, the progressive and the resolving. To confirm this diagnosis it was necessary to exclude congenital abnormalities. It was noted that the progressive type usually occurred in the thoracic region in the male and also that they were usually left-handed curves; commonly the major curve was found between the fifth and the twelfth thoracic vertebræ. The resolving type was the combined thoracic and lumbar curve. The prognosis was better for this than for the single thoracic curve. There were also thoraco-lumbar and lumbar curves, but these were very few. The resolving infantile curve was usually noticed between the fourth and tenth months and usually disappeared in the first few years of life. An early differential diagnosis between these two types of curve is essential, the one being innocent and the other so malignant. The only single feature that appears to help in the diagnosis is that the presence of compensatory curves usually indicates that the curve is of a progressive type. The author does not discuss the treatment of this condition in detail, but he notes that operative correction and fusion cannot be made until ten years of age, and that it is usually required. Until then, a Milwaukee jacket has been found to be the best method of preventing deterioration. Usually, the child is not old enough to wear a Milwaukee-type jacket until about the age of three and a half years. For patients younger than this, a Risser jacket correction followed by application of plaster jackets is under trial.

Lambrinudi's Arthrodesis.

I. G. MACKENZIE (*J. Bone Jt Surg.*, November, 1959) has examined the records of 182 operations for Lambrinudi's arthrodesis performed at the Royal National Orthopædic Hospital, London. It was possible to trace and examine 100

of these patients, a follow up rate of 55%. The results were graded into four groups: (i) ideal; (ii) good; (iii) fair; (iv) failed. The author was prompted to review these cases because of poor figures reported in reviews by other authors. The operation was described by Lambrinudi in 1927 as an operation to correct foot drop. He had expressed satisfaction with the result but had not given any details. The operation became popular and indications were extended to include equino-varus, equino-valgus and even cavus deformities, as well as the fixed equinus and the passively correctable drop foot for which it was originally intended. The author's series include a number of patients operated on by Lambrinudi himself. A number of complications are reported. The early complication of delay in healing occurred frequently. Sepsis did not appear to affect the ultimate result. The late results showed instability caused by stretching of the lateral ligament and the anterior ligaments of the ankle as a serious cause of failure. In some cases this has led to the need of a later arthrodesis. Another complication was the development of callosities due to altered weight-bearing points on the sole of the foot. Arthritis has occurred in the ankle joint. Pseudarthrosis occurred more often in the older age group. The final listing is that 57% were successful, 19% were failures. Many of these failures, however, were associated with faulty technique.

Fracture Dislocation of the Lumbar Spine.

F. R. ZADIK (*J. Bone Jt Surg.*, November, 1959) describes and figures a new appliance for use in the internal fixation of fracture dislocation of the spine. This apparatus is simple and is stated to make firm internal fixation easy. The author considers that it is much more effective, easier to apply, and less likely to slip than the plate which has been used at Sheffield and elsewhere in the management of patients suffering from paraplegia with spinal cord damage after fracture dislocation of the spine.

PÆDIATRICS.

Tracheostomy in Infants and Children.

L. R. RUBIN, B. E. BROMBERG AND R. H. WALDEN (*Amer. J. Surg.*, December, 1959) have investigated the reasons for high mortality and morbidity rates associated with tracheostomy in infants and children. Although the indications for tracheostomy remain unchanged at all ages, the margin of safety is reduced with decreasing age, and the period for elective operation is shorter. Infants have small airways and high metabolic requirements and handle their pharyngeal and tracheo-bronchial secretions poorly. Practically all standard tracheostomy tubes for use in infants and children are excessive in length and readily cause obstruction at the carina. In no instance should they be longer than 5·5 cm. The 90° tube, although unsatisfactory in some instances, still possesses the best arc. The diameter of the tube should be sufficiently smaller than the trachea itself to permit ample breathing space when the tube is corked. The authors give a detailed account of operative technique and post-operative care. Serious consideration must be given to the performance of an elective tracheostomy in the following situations: (i) when there has been a difficult endotracheal intubation; (ii) in surgical operations about the pharynx, larynx, tongue or mandible, when permanent or temporary respiratory obstruction may be a consequence; (iii) in prolonged comatose states; and (iv) in cases of trauma to the respiratory tract or lungs, such as burns, when efficient respiratory toilet is essential.

Encopresis.

W. M. EASSON (*Canad. med. Ass. J.*, March 19, 1960) discusses fæcal soiling in children, not caused by organic defect or illness, in the light of 15 cases occurring in his practice. Psychotic children were excluded from the study. These children ranged in age from two to 12 years, and all but two were boys. This male preponderance has been noted by other writers. The author classifies encopresis into primary encopresis, occurring in children who have never been toilet-trained, and secondary encopresis, when it occurs in children who have been bowel-trained but have regressed. Each category may be subdivided into those with an infantile pattern of soiling, and reactive cases, in which soiling is caused by fæcal leakage in a syndrome of chronic constipation. The author concludes that children who soil in a regressed infantile fashion usually achieve a symptomatic cure in response to supportive, approving treatment, which can well be undertaken by the family doctor or pædiatrician. However, reactive encopresis indicates much more serious family psychopathology, and patients in this category and their families require intensive and often prolonged treatment. The author believes that this is usually best undertaken in a psychiatric setting.

Salicylism Treated with Sodium Bicarbonate.

T. OLIVER AND M. DYER (*A.M.A. J. Dis. Child.*, May, 1960) state that the ingestion of toxic quantities of salicylate results in alterations of acid/base homœostasis which at times may be profound. The pathogenic mechanisms include hyperventilation secondary to respiratory stimulation, increase in metabolic rate, and disturbances in carbohydrate and lipid metabolism. Further alterations frequently follow the vomiting and dehydration which are so often associated with ingestion of very large amounts of salicylate. There is no specific antidote for salicylism. Treatment is currently aimed at augmenting the elimination of salicylate via the urine or, in severer cases, directly from the blood by hæmodialysis or exchange transfusion. Thirty-eight children ranging in age from 14 to 48 months were studied after the accidental ingestion of salicylate compounds. The intravenous administration of sodium bicarbonate in a dose of 3·5 to 5·0 mEq. per kilogram resulted in an alkaline urine in 15 of the 18 patients so treated. In these 15 a significantly more rapid drop in serum salicylate occurred than in two control groups who received fluids alone. These studies confirm the fact that marked salicyluria can be achieved by alkalinization of the urine. At the same time they establish the fact that the theoretical danger of alkalæmia as the result of bicarbonate loading with the dosage used in this study did not occur, nor would it be expected in view of the initial acid/base balance. All of these patients had some degree of metabolic acidosis when first studied. Because metabolic acidosis occurs irregularly, if at all, in older children with salicylism, the intravenous administration of sodium bicarbonate should be limited to children less than four years of age. Because of the tendency for serum potassium to fall, particularly during sodium loading, it is recommended that potassium in a dose of 80 to 120 mEq. per square metre per 24 hours be added to the intravenous solution once it is established that the kidneys are functioning. Urine pH should be determined frequently, and additional bicarbonate given if the urine does not become alkaline within four hours after the initiation of therapy. The rapid fall of serum salicylate levels suggests that the careful use of sodium bicarbonate is the preferred treatment of salicylism in children less than four years of age.

Acute Bacterial Meningitis.

R. HAGGERTY AND M. ZIAI (*Pediatrics*, May, 1960) state there is a difference of opinion over several aspects of management of acute bacterial meningitis in children, including the selection of the optimal antibacterial regimen to achieve the lowest rates of mortality and sequelæ. While few would deny that the use of a single effective antimicrobial agent is theoretically ideal, practical difficulties in the application of this theory remain. The most difficult problem is prompt identification of the ætiological agent. In nearly 50% of patients with bacterial meningitis the initial smear of cerebrospinal fluid fails to yield a correct ætiological diagnosis. Clinicians face a dilemma in these cases, for prompt institution of therapy is essential if one is to reduce mortality and sequelæ. And yet, no single antimicrobial drug provides optimal treatment for all three of the most common bacterial agents causing meningitis in children (*Pneumococcus*, *Meningococcus* and *Hæmophilus influenzæ*). A controlled study of the treatment of bacterial meningitis with single and multiple, potentially antagonistic, antimicrobial drugs was undertaken. Sixty-five patients received a single drug and 71 received several drugs in combination. The two groups were generally comparable. There was no significant difference in the results, i.e. antagonism could not be demonstrated in this clinical study. The results of the study indicate that, when the ætiological agent of bacterial meningitis is promptly identified, the use of a single antimicrobial agent most likely to be effective is the wisest course. It also indicates that, in patients over one month of age with acute primary bacterial meningitis in whom an ætiological agent cannot be promptly identified, the use of multiple drugs aimed at the three most likely organisms can be employed without danger of clinically apparent antagonism.

Brush Up Your Medicine.

ESSENTIAL HYPERTENSION.[1]

For practical purposes a resting blood pressure which is consistently 160/100 mm. of mercury, or higher, is abnormal at any age, but this does not imply that it is of serious significance or that treatment is required. For correct assessment a period of observation is often necessary. A pressure of 160/100 mm. of mercury is, by itself, unlikely to cause symptoms or to be associated with objective evidence of hypertensive disease.

Systolic hypertension may occur with anxiety, aortic incompetence, thyrotoxicosis or heart block, but is most frequently attributable to atherosclerosis decreasing the elasticity of the aorta and its main branches. This may also lower the diastolic pressure, leading to an increase in pulse pressure. As a general rule, systolic hypertension does not require treatment with hypotensive drugs, and it should be remembered that when the blood pressure of atherosclerotic patients is lowered, they are more liable to cerebrovascular accidents from thrombosis.

Diastolic hypertension is due to increase in peripheral resistance and is the syndrome more often associated with hypertensive disease.

As essential hypertension is a primary condition, the diagnosis can be made only after excluding conditions to which the raised blood pressure may be secondary, i.e., renal disease (most common), coarctation of the aorta, phæochromocytoma, Cushing's syndrome, polyarteritis nodosa, aldosteronism, toxæmia of pregnancy, etc.

The main decision which has to be made is whether the patient merely has high blood pressure or whether there is evidence of secondary hypertensive disease, and, if so, whether it is mild, moderate or severe. Though atherosclerosis and hypertension are often associated, there is no evidence that they have either a common basis or a common ætiology.

Symptoms and Signs.

Headache, vertigo, restlessness, irritability, etc., may be present, and it may be difficult to decide whether they are directly attributable to the hypertension alone or to hypertensive cardiovascular disease with manifestations primarily in heart, brain, retina and kidneys, as follows:

Heart: Dyspnœa on exertion, paroxysmal nocturnal dyspnœa, cardiac pain, left ventricular hypertrophy, accentuated aortic second sound, cardiac failure.

Brain: Hypertensive encephalopathy, cerebral hæmorrhage or cerebral thrombosis (major or minor episodes), mental changes.

Retina: Grade I—general narrowing of the arterioles with varying calibre and increased light reflex; Grade II—further reduction in calibre and constriction of the veins where crossed by the arterioles; Grade III—the addition of exudates and/or hæmorrhages; Grade IV—papilloedema.

Kidneys: In hypertensive cardio-vascular disease functional insufficiency is evident much earlier in the heart, retina and brain than in the kidneys. Although impairment of renal function is a feature of hypertensive disease, most patients will die of cardiac failure or of a cerebro-vascular accident. As a reasonable guide to the degree of impairment of renal function the following tests are important: (i) Specific gravity concentration test, (ii) estimation of creatinine clearance, (iii) blood urea estimation (for assessment of renal failure), (iv) renal biopsy in difficult cases. Pyelography in a patient under the age of 50 years is necessary to exclude unilateral renal disease.

Taking the Blood Pressure.

In patients under treatment with ganglion-blocking drugs, the blood pressure must be recorded both in the supine and in the standing positions. These drugs have little, if any, central effect, and their action depends mainly on posture, therefore pressure readings are valueless under these conditions if taken with the patient in the supine position alone.

Treatment.

Probably not more than 10% of persons with blood pressure of 160/100 mm. of mercury or over require treatment, and in the elderly hypertension can usually be ignored. Treatment should be considered whenever there is objective evidence of hypertensive disease and in young adult males with considerable diastolic hypertension and a bad family history. It should always be instituted if there is evidence of progression under observation for a short period, e.g., 6 to 12 months.

The aim is to reduce the blood pressure without undue side effects, and caution is required when coronary or cerebral atheroma is suspected, or when renal function is considerably impaired.

A. Ganglion-Blocking Drugs: Oral.

The following ganglion-blocking drugs are given by mouth.[1]

1. Hexamethonium. This is now superseded by pentolinium, mecamylamine, chlorisondamine, etc.

2. Pentolinium tartrate ("Ansolysen") (40 mg. and 200 mg. tablets). Dosage is commenced with 20 mg. three times a day and increased by 20 mg. increments to each dose.

3. Mecamylamine ("Mevasine") (2·5 mg. and 10 mg. tablets). Dosage is commenced with 2·5 mg. three times a day and increased by 2·5 mg. increments to each dose. Currently this is the most popular drug in this group.

4. Chlorisondamine ("Ecolid") (50 mg. tablets). Dosage is commenced with 25 mg. three times a day and increased by 25 mg. increments to each dose.

5. Pentacynium ("Presidal") (100 mg. tablets). Dosage is commenced with 50 mg. three times a day and increased by 50 mg. increments to each dose.

If this regime fails to reduce the blood pressure without undue side effects, the following steps should be considered: (i) add neostigmine; (ii) reduce the dose of the ganglion-blocking drug, and add chlorothiazide; (iii) if this fails, reduce the salt intake and consider the addition of one of the rauwolfia compounds.

The efficacy of the ganglion-blocking drugs can be judged only from blood pressures taken when the patient is erect.

Side Effects.—Side effects (due to parasympathetic blockage) are postural hypotension, blurring of vision, dry mouth, distension with constipation, diarrhœa, retention of urine and impotence. Sudden cessation of treatment may be dangerous, the overshoot resulting in intracranial hæmorrhage.

Contraindication.—Ganglion-blocking drugs are contraindicated for patients with a previous history or family history of depression. Time spent in eliciting this information is well worth the trouble.

B. Non-Mercurial Diuretics.

Non-mercurial diuretics, such as chlorothiazide, enhance the effect of ganglion-blocking drugs and allow their dosage to be reduced, with a corresponding reduction in side effects.

Current practice is: (*a*) halve the dose of the ganglion-blocking drug; (*b*) add chlorothiazide, 250 mg. three times a day; (c) then gradually increase the dosage of the ganglion-blocking drug as required.

This diuretic action of chlorothiazide is useful in patients with cardiac failure. A supplement of potassium chloride is occasionaly necessary.

C. Rauwolfia.

The rauwolfia alkaloids have a central inhibitory action, especially on the brain stem, and produce a fall in blood pressure, bradycardia and sedation. They are often given with ganglion-blocking drugs so that the dosage of the latter may be reduced and side-effects lessened. The hypotensive action of rauwolfia is so mild, however, that given alone it is effective chiefly in nervous people with labile hypertension who require a sedative.

Side effects are common, particularly with reserpine.

Some physicians advocate reserpine and chlorothiazide or one of the other non-mercurial diuretics before resorting to a ganglion-blocking drug. The hypertensive receiving

[1] No. 6 of a series of synopses prepared by Dr. Alex Johnson of Canberra, in collaboration with the Australian College of General Practitioners. Each synopsis has been submitted for approval to a leading member of the College, to a professor of pharmacology and to a specialist in the field concerned.

[1] Bretylium tosylate ("Darenthin"), which has been recently introduced, is not strictly a ganglion-blocking drug but may be conveniently considered with this group. Dosage is commenced with 200 mg. three times a day and increased by 100 mg. increments to each dose.

reserpine often has quite severe falls in blood pressure from chlorothiazide in minimal dosage.

D. Hydrallazine.

Hydrallazine has central and peripheral action but is not a ganglion-blocking agent. Unique among the hypotensive drugs, it increases cardiac output and lowers the blood pressure simultaneously. Toxic effects are frequent and severe. Optimum indications are when renal function is impaired and avoidance of further depression of renal blood flow is desired.

E. Veriloid and Protoveratrines.

Veriloid and proteveratrines are of little value in treatment.

F. Surgical Operation.

Sympathectomy is indicated only when the blood pressure cannot be controlled satisfactorily by medical treatment. Adrenalectomy is rarely required.

G. General Management.

Moderation is important in all things—work and play, rest and exercise, diet and smoking, salt intake, etc.

The patient should reduce weight if obese.

Patients with essential hypertension are grateful for relief of symptoms such as headaches, dyspnœa or angina, but it should be remembered that their general health is unaffected.

By contrast many patients under treatment with any of the modern hypotensive drugs do not feel well, quite apart from specific side effects such as dry mouth or postural hypotension.

Once begun, treatment should be continued indefinitely.

N.B.—Several leading authorities in cardiovascular disease are convinced that many patients with hypertension are receiving treatment which is unnecessary and many others are receiving therapy which is inadequate.

Reference.

R. W. D. TURNER (1959), "Diagnosis and Treatment of Essential Hypertension", *Lancet*, 1: 897.

ALEX JOHNSON,
Canberra.

Out of the Past.

PUBLIC CHARITIES.[1]

[Extracts from "The Public Charities and their Abuses", by James Jamieson, *Victorian Review*, May, 1880.]

FROM the outsider's, i.e., the non-committeeman's point of view, it is a matter for something quite different from congratulation, that, in a community like this, there should be such a large amount of eleemosynary relief given, even of a strictly medical sort. Supposing all the applicants to be deserving of assistance, it would be painful enough, but would have to be borne as inevitable. If, on the contrary, it be true, as is commonly supposed, that quite a considerable proportion of those admitted to the benefits of our hospitals might pay for what they receive, a burden is unfairly laid on those who, directly or indirectly, provide those benefits; because instead of doing good purely and simply, as originally intended, their contributions go towards pauperising whole classes in the community. A man, who begins by improperly getting medical relief at the public expense, is likely enough before long, if convenience or increased greed enjoin, to look for more material assistance, and take food and clothing, if obtainable. With reference to the vexed question of imposition on the medical charities, I can only give it as my decided opinion, based on personal contact with the patients, that quite a considerable proportion of those, who now get professional advice and medicines free, could pay something. I believe that this opinion is shared by every medical man on the staffs of the hospitals and public dispensaries of this city. There is, in fact, no more insidious beginning to a habit of clinging to the skirts of charity, than is allowed by our free and easy way of giving admission to the benefits of these institutions. For while hospitals are not by any means the only charities, capable of doing much unmixed good, or much harm, according to the mode of administration, they are in many ways the most important for good or ill. People may palm off their broken down relatives, or helpless children on Benevolent Asylums or Charity Schools; but that is a very deliberate form of imposition, and in its very nature more exposed to the risk of detection. For its perpetration some training will very often be required, and that training may readily be got by habitually throwing the burden of caring for helpless dependants, in times of sickness, on the hospital authorities. Becoming an out or in-patient, though able to pay, evidently is, in the popular eye, a very venial offence, though it is difficult in principle to draw the line between becoming unworthily a recipient for temporary illness and doing so for a longer period when disablement is lasting.

From whatever causes, and these may be many and varied, it is certain, that the multiplication and extension of public charities of any sort tend to encourage applications to them. It may be in part owing to the less inconvenience attendant on making such application to a place within easy reach, or because those at the head of a new institution open its doors widely, so that, by being able to show work done, they may both establish its *raison d'être*, and have a claim to continued or increased support. The fact of this increased supply creating a demand is clearly shown in the history of the Melbourne Benevolent Asylum. In the report of the Royal Commission on charitable institutions, issued in 1870, it is stated that the asylum had erected two new wings, so that it contained 533 inmates in 1869, as against 312 in 1861, and the remark is then made: "And we here deem it deserving of observation, as a significant fact, that this additional accommodation was no sooner completed than the candidates for admission exceeded the power and means of reception . . . ." That there is need of something of the nature of a hospital for paying patients in this city is generally allowed. It would meet the case of a good many who are not, and do not wish to be, objects of charity, and yet in time of sickness cannot obtain right nursing and home comforts. That its establishment would materially diminish the number of claims for admission to the free hospitals I do not believe, though it might do so to some extent, and it would take away an excuse for imposition. Some of the country hospitals now admit paying patients; but the only one in Melbourne which tries to combine the free and the pay principles is the Homœopathic Hospital, which in 1879 derived £358.2.6 from in and out patients. This instance notwithstanding, it is probable that any experiment of the sort on a large scale would have the best chance of success, if entirely separate from any of the free hospitals at present in existence. The Home Hospital Association, which has lately been established in London, has taken up this position, declining the offer of one of the blocks of St. Thomas's Hospital at the low rental of £300. As with the dispensaries, it may be regarded as essential to the success of any pay hospital, that it should have the hearty support of the medical profession. If there is any suspicion that free, or inadequately remunerated medical attendance is expected, for persons well able to pay; or that the interests of any small number of medical men are to be furthered at the expense of the rest; then failure or imperfect success may be predicted. Though essentially a commercial enterprise, which would no doubt pay in the long run, it is not at all likely that there would be immediate profit; and those willing to advance the necessary funds might, in the absence of dividends for a time, console themselves with the thought that they were furthering a truly benevolent project, though the recipients of the benefits were expected to make an adequate payment for them.

So much for the provision of means, whereby excuse would be taken from those who now may plead that, though unwilling to impose on the public charities, they are compelled to do so, for want of some other resource suited to their means. That some more direct check ought to be put in operation, whether or not the self-supporting institutions are called into existence, is to all but committeemen very obvious. The wrangling and difficulties that have arisen over the proposal to appoint an inspector to inquire into the circumstances of applicants for relief show how needful it is to bring outside pressure to bear on the average managing committee. If general action is not taken in this matter without delay, it will clearly be the duty of the subscribers and governors of the different charities to elect only those who declare their determination to aid in putting

[1] From the original in the Mitchell Library, Sydney.

a stop to abuses, in that or some more effectual way. Seeing, however, the comparatively slight interest taken by the subscribers in such questions, it might fairly be expected that the Government, as chief contributor, should insist on having all due guarantees that its funds are properly expended. The intimation that State endowment would be withheld from those charities which neglected to make proper investigations would put an end to delays and obstructions.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings of the House of Representatives.

May 12, 1960.

Immigration.

MR. FOX: Has the Minister for Immigration seen a report attributed to the Reverend W. J. Hobbin, chairman of the Australian National Committee for the United Nations World Refugee Year, to the effect that Australia's practice of selecting only the youngest, healthiest and most highly skilled migrants has resulted in thousands of people who now need assistance being left behind in refugee camps? Can the Minister say whether it is possible for Australia to absorb larger numbers of physically handicapped persons from refugee camps in Europe?

MR. DOWNER: I have seen a report of the statement attributed to the reverend gentleman to whom the honorable member has referred. I do not think that we really have anything to be ashamed of in our contribution to the re-settlement of refugees. Taking the over-all aspect of the matter, in comparison with our population, Australia has done more to help in the re-settlement of refugees than has any other country in the world. In absolute terms, we are second in total intake only to the United States of America.

As for the particular point to which my honorable friend referred, we are giving in this World Refugee Year particular attention to the problem of the residual refugee in the camps in Europe, and particularly to those who are suffering from some physical handicap. The honorable gentleman might remember that, during the Australian Citizenship Convention last January, I announced on behalf of the Government the further steps we were taking in this respect. This, of course, Mr. Speaker, is a continuing matter. The Government has not said the last word in this respect. The honorable gentleman might remember that, only two or three weeks ago, I announced that we had gone one stage further, and on behalf of the Government, I announced that we had now made provisions for bringing into Australia thirteen cases of tuberculosis sufferers, including some members of family units, involving 22 persons in all. I give that to the honorable gentleman as an example of the Government's thinking, and of how we are certainly not content at this stage with all we have done, but are continually looking to the future to see what we can usefuly do to solve this very sad problem.

Health and Medical Services.

MR. REYNOLDS: In the absence of the Minister for Health, I direct my question to the Acting Prime Minister. Is the right honorable gentleman aware that New South Wales doctors, in a secret ballot which has just been conducted by the British Medical Association, have voted four to one against co-operating with the Government in its amended pharmaceutical benefits scheme? Is he aware also of considerable public dissatisfaction which has arisen from the discovery that the range of drugs on the 5s. list is not as wide as the public was led to believe? Further, is he aware that considerable confusion exists in the administration of the scheme due to the absence of preliminary consultation with State departments of health and doctors' and chemists' professional organizations? In these circumstances, and in view of the threats to the continuance of the scheme, will the Government make a thorough and urgent review of the scheme?

MR. MCEWEN: In the absence of my distinguished colleague, the Minister for Health, who, I am sure, enjoys the confidence of the medical fraternity in Australia, I am only able to say that I believe that the attitude of the medical fraternity to the Government's health scheme will be determined, not by State organizations but by the Federal Council —if that is the correct term—of the British Medical Association. We have a long experience in this federation of ours of governmental, industrial or professional organizations in the single States differing on occasions from what turns out to be the majority over-all Australian attitude.

I am highly confident that the doctors in Australia will cooperate with the Government at all times in its high purpose, which it shares with the Opposition, of seeing that appropriate facilities are available for attending to the health of the people. The Government continuously has followed the practice of close consultation with those whom it calls upon or invites to work with it in pursuance of general policies for the good of Australia.

May 17, 1960.

Pensioner Medical Services.

MR. WHITLAM asked the Minister for Health, upon notice:

What arrangements has his department made with the States concerning charges for hospital treatment for pensioners?

DR. DONALD CAMERON: The following is the answer to the honorable member's question:

It has been a long standing practice for State governments to provide free hospital treatment for pensioners. The Commonwealth pays the State 12s. per day for each bed occupied by pensioners who are not insured with registered hospital benefits organizations. Recently there has been some departure in some States from the traditional policy of providing free hospital treatment for pensioners. The basis of Commonwealth payments has, however, continued unaltered.

May 18, 1960.

Lung Cancer.

MR. PEARCE: I ask the Minister for Health whether the National Health and Medical Research Council, at its recent meeting, expressed itself as strongly of the opinion that cigarette smoking was a contributory cause of lung cancer. Did it consider that steps should be taken to publicize this fact? Has there been an increase in the incidence of lung cancer in Australia in recent years?

DR. DONALD CAMERON: Perhaps I should first of all remind the House that the National Health and Medical Research Council has been set up to advise, not only the Commonwealth Government, but all State Governments. It has considered the relationship between smoking and lung cancer on several occasions. At its meeting in Canberra last week it again considered this question and expressed the opinion that there was strong contributory causal relationship between cigarette smoking and lung cancer. Perhaps it is fair to say that some authorities do not agree with this view, but the body which advises the Government believes that smoking is a very important contributory cause. There has in fact been a steep increase in the incidence of lung cancer in Australia in recent years, both relatively and absolutely. The National Health and Medical Research Council went further than that. It was of the opinion that these facts should be publicized and, indeed, that it might be advisable for Australian governments to consider whether steps should be taken to control in some way advertising designed to promote smoking.

May 19, 1960.

Coronary Occlusions in Ex-Servicemen.

MR. CHANEY asked the Minister representing the Minister for Repatriation, upon notice:

1. Are statistics kept by the Repatriation Department of the number of ex-servicemen who have died from coronary occlusion?

2. If so, what is the (*a*) total number of ex-servicemen; (*b*) number of ex-servicemen of World War II; and (*c*) number of ex-servicemen since 1945 under the age of 35 years who have died from this cause?

DR. DONALD CAMERON: In reply I wish to furnish the following answers:

1. Yes, but the statistics are incomplete in the following respects. The records of the department cover only those ex-servicemen who have had an incapacity accepted as due to war service, and those whose dependants have claimed death as due to war service. Further, the cause of death of 1914 War ex-servicemen has only been recorded since January, 1959.

2. Answers to this question are: (*a*) for reasons explained in 1, the total number of ex-servicemen who have died from coronary occlusion is not known; (*b*) there have been 1,714 recorded deaths of World War II ex-servicemen; (*c*) this information is not available.

3. I might add that from 15th January, 1959, there have been 771 recorded deaths from coronary occlusion of ex-servicemen from World War I.

Pensioner Medical Service.

MR. JONES asked the Minister for Social Services, upon notice:

1. How many pensioner wives are eligible for the benefits of the free Pensioner Medical Service?

2. What is the annual cost of this service?

DR. DONALD CAMERON: The Minister for Social Services has referred this question to me for attention, and I furnish the following answer:

1. This information is not available.

2. The cost of medical services rendered to all pensioners and their dependants enrolled in the Pensioner Medical Service during the financial year 1958-59 was £3,806,467.

May 31, 1960.

Penicillin.

MR. KILLEN: I address a question without notice to the Minister for Health. I refer the honorable gentleman to a recent survey the results of which were published by the National Health and Medical Research Council, in which the council stated that in the absence of information concerning the resistance of infections, penicillin should not be used in serious staphylococcal infectious cases. I ask the honorable gentleman what steps he has taken to ensure that the medical profession is aware of that fact. Can the honorable gentleman say whether the breakdown of the effectiveness of penicillin has been due to indiscriminate use of this preparation? Further, can the honorable gentleman say whether or not antibiotics generally are being used in an indiscriminate fashion.

DR. DONALD CAMERON: A survey has recently been made by the Commonwealth Department of Health of penicillin resistance and the use of penicillin in staphylococcal infections. A report has been issued and is being circulated to the medical profession. In addition, quite a large amount of information on this subject is published with considerable regularity, in various medical and scientific journals. I do not know that it is possible to say that resistance of organisms to penicillin is due entirely to the indiscriminate use of penicillin. However it is, I think, obvious that not only penicillin, but also other antibiotics, need to be used with care not only in the treatment of staphylococcal infections, but in the treatment of all infections. The honorable gentleman is probably aware that the use of antibiotics, at any rate insofar as they are pharmaceutical benefits, is regulated by the Commonwealth Government on the advice of its expert committee on pharmaceutical benefits.

SENATE.

THE following extracts from *Hansard* relate to the proceedings of the Senate.

May 11, 1960.

Medical Benefits Scheme.

SENATOR ARNOLD asked the Minister representing the Minister for Health, upon notice:

How many doctors received payments under the medical benefits scheme during 1958-59?

SENATOR HENTY: The Minister for Health has furnished the following reply:

Under the medical benefits scheme payments of Commonwealth medical benefit are made to contributors to registered medical benefits organizations. Approximately 5500 doctors received payments from the Commonwealth under the pensioner medical service.

May 18, 1960.

Pharmaceutical Benefits.

SENATOR PEARSON: Has the Minister representing the Minister for Health any reply to a question I asked on 31st March last regarding the availability of the drug rastinon under the new pharmaceutical benefits scheme?

SENATOR HENTY: My colleague, the Minister for Health, has advised me that rastinon tablets have always been available as a pharmaceutical benefit, but only to pensioners. Under the new pharmaceutical scheme, as from 1st March, 1960, they will be available as a pharmaceutical benefit to the community as a whole.

Commonwealth Serum Laboratories.

SENATOR PEARSON asked the Minister representing the Minister for Health, upon notice:

1. Did the Commonwealth Serum Laboratories make a substantial profit in the financial year, 1958-59?

2. If so, what was the amount of the profit?

3. What percentage of the national health expenditure is directly attributable to the use of antibiotics?

4. What percentage of this cost is spent on "broad spectrums"?

5. Is the Government taking any steps to obtain a licence for the manufacture by the Commonwealth Serum Laboratories of these "broad spectrums", which have hitherto been imported from the United States of America, or other overseas sources?

6. If necessary, what steps can be taken by the Commonwealth to enforce the granting of a licence to Australia for this purpose?

SENATOR HENTY: The Minister for Health has now furnished the following replies:

1. and 2. For the year 1958-59 the Commonwealth Serum Laboratories made a profit of £212,007.

3. In 1958-59, approximately 50 per cent. of the expenditure on pharmaceutical benefits.

4. Approximately 58 per cent.

5. As and when required, steps are taken to obtain licences from overseas manufacturers to enable the Commonwealth Serum Laboratories to manufacture biological products. The advisability of manufacturing broad spectrum antibiotics is, of course, kept in mind in these considerations.

6. If a situation arose in which the Commonwealth thought it was necessary to manufacture a product and it was in a position to manufacture the product, the Commonwealth could invoke Section 125 of the *Patents Act*, under which the Commonwealth may make use of an invention, subject to the payment of compensation.

Hospital and Medical Benefits.

SENATOR O'FLAHERTY asked the Minister representing the Minister for Health, upon notice:

1. Is it a fact that to date South Australian railway employees have been provided with full hospital treatment amongst other things, without any further payment, by a non-profit sickness and hospital benefits organization to which they contribute four hours' pay per annum, and retired employees 5d. per week.

2. Is it also a fact that owing to the altered incidence by the Federal Government in respect of hospital and medical reimbursements and/or subsidies, this organization has been notified that it has now to charge 7d. per week, representing an increase of 40 per cent., in the contributions payable by the retired employees, who, in some cases, are also pensioners?

3. Will the Minister have a quick investigation to see whether it is not possible for his railway employees' organization to go on supplying free hospital treatment at least without increasing the charges to retired employees?

SENATOR HENTY: The Minister for Health has now furnished the following replies:

1. The Commonwealth and fund hospital benefits provided through the South Australian Railway Employees' Hospital Fund covered the cost of public ward hospital treatment in South Australia prior to the recent increase in charges made by the South Australian Government. The contribution payable by retired employees is 5d. per fortnight.

2. No. I understand that the organization is considering the effect of the increased hospital charges upon its financial position. However, as yet the organization has not submitted to the Department of Health any proposal for increase in contribution or benefits. The department has not issued any notice to the organization requiring it to increase contributions

3. The question of the contributions payable by members is essentially a matter for determination by the organization,

Any proposal for an increase in contributions will be thoroughly investigated by the Commonwealth Actuary and the Department of Health, before the organization can put them into effect.

May 19, 1960.

Fluoridation of Water.

SENATOR KENDALL asked the Minister representing the Minister for Health, upon notice:

1. Has the Minister seen a report of evidence given before the Royal Commission on Fluoridation, at present sitting at Toronto, in which Dr. Charles Brusch stated that "fluorine could cause damage to the brain, premature birth and paralysis of nerve ends", and also that "there was complete evidence that the Nazis used fluorine in brain washing processes"?

2. In view of the fact that some local authorities in Australia are considering the introduction of fluorine into drinking water, will the Minister consider bringing down legislation banning its use until such time as scientists have reached a firm decision on this controversial matter, or at least until the findings of the present royal commission now sitting in Canada are available for complete examination?

SENATOR HENTY: The Minister for Health has furnished the following reply:

1. No, but I have examined similar statements which have been published from time to time.

2. Fluorine, like chlorine, iodine and bromine, all of which are consumed at some time or other by most people, could be harmful if more than a certain level of dosage were to be taken. If fluorine is consumed in drinking water at the level of one part per million of water, it has been shown in many experiments and as a result of intensive investigation to be a safe and effective measure for the partial prevention of dental caries. Its use for this purpose has been recommended by the National Health and Medical Research Council. Whether or not the various States decide to act on this recommendation is a matter for each State to determine.

Correspondence.

THE ORGANIZATION OF THE PROFESSION.

SIR: Acting under powers arising out of their respective constitution and by-laws, the Federal Council and New South Wales Branch of the British Medical Association have made and are able to make decisions vitally important to their respective members. It is reasonable to suppose that the State Councils of the other States have similar powers. In regard to the Federal Council, the saving grace is that its members are expected to vote in accordance with their respective State Councils' decision.

The above facts have been amply demonstrated on several occasions, and more recently by the Federal Council agreeing to recommend to members the acceptance of the recent National Health formulary. This apparently has been met with marked disfavour by many of the profession; however, having regard to the cumbersome machinery for general rejection of such decisions, particularly that provided for in the N.S.W. Branch's constitution, these agreements were in fact a *fait accompli*.

We have previously stated that the N.S.W. Council is vitally a law unto itself; under its constitution it can make decisions affecting every member; nothing in either its constitution and by-laws provides a course of action so that members can force the Council to act in accordance with the wishes of its members. An extraordinary meeting of the Branch has only an advisory power, and at such meetings no provision is made for proxy voting.

At meetings of the Council voting is necessarily the result of personal opinions of the individual members, and with very few exceptions (civil service, women and local association representatives) never by any direction of any special group of members of the Branch. Of course, if grave dissatisfaction exists amongst members they do possess the power to appoint a new Council at the annual election.

The above preamble is necessary in view of the proposed formation of the Australian Medical Association. It is known that the process of formation of the articles of association, constitution and by-laws of the Federal and State Branches of this body is in process. As it at present stands, if members do not take an immediate stand, this again may be a *fait accompli*. No draft of the above has been circulated to any local association or Section of the N.S.W. Branch, nor has any suggestion been made that there will be any vital alteration in them, more particularly in regard to the method of election of the Council; in fact, the views of present members would appear to be hardly worthy of consideration.

At present there appears to be a general fear of the possibility of a nationalized medical service; if the methods of election of State Councils in the proposed Australian Medical Association is to remain unaltered, then this fear would be increased, as State and Federal Council would possess the power of making decisions without consulting members of the profession. It is not suggested that the Councils would make such decisions without endeavouring to first of all obtain the opinions of its members on important matters of policy; but the present method of obtaining this through extraordinary meetings—local associations, special sections and plebiscites—is cumbrous and time-consuming and, in view of the present apathy of members, often indefinite.

For Councils to be truly representative of its members there is only one method—namely, that the members of Council should be elected from groups whether they be local asociations, special sections, civil service and so on. If this were followed, voting in Council matters would be by direction, and the present Annual Meeting of Delegates, plebiscites and extraordinary meetings of the Branch would be unnecessary; it is felt that this method of Council elections would be a grand step in removing the present apathy of members.

One other point: surely members of Branches, not their respective Councils, should elect their Federal representatives; and surely the Branches can afford to meet all necessary expenses, including those of *locum tenentes*, to Federal and State Councils.

It is time and timely that the obsolescent constitution and by-laws be modernized, not only to provide for modern ideas, but more particularly for future emergencies; it is essential that when representatives of either the Federal Council or State Councils speak, they really speak with the majority opinions of its members. As it at present stands, they may do so, but more likely their opinions are only guess work. True opinions can only be obtained by Council when its members are instructed by and are responsible to their groups.

It is the responsibility of all members for their future professional and economic welfare to insist upon a democratic method of election of their respective Councils.

Yours, etc.,

CARL H. JAEDE,
C. B. INGLE.

4 Robey Street,
Mascot,
New South Wales.
July 12, 1960.

TRACHOMA IN WESTERN AUSTRALIA.

SIR: Your recent leader on the above aroused much attention among ophthalmologists, especially those who have sojourned in endemic areas such as Polynesia.

Apparently the form of the disease among aborigines is accompanied with secondary infection, much like that seen in Egypt, and described by Maxwell Lyons and others. Dust, flies, filth, etc., will account for this type of trachoma.

Now, the Polynesians are a very clean and highly civilized race and free from the neuroses of the twentieth century. They have their *Tambuas* (taboos), of course, but a form of granular conjunctivitis is among 40% of the races—Melanesian, Polynesian and Micronesian.

The following racial custom is prevalent among the Fijians and Samoans. To keep the hut (*bure*) warm and for cooking purposes, they light a small fire within the precincts of the hut, and as the windows are closed up, the exit for the resulting smoke is limited. Hence most Fijians have chronic catarrh and sore eyes of a granular nature.

The Indian and Chinese races, who form a good 50% of the community in the South-West Pacific, do not

light fires within their shacks, but outside. The result is that in the records, "trachoma" is far less prevalent among them.

The absence of flies is very noticeable, as is also the absence of marked scarring of the cornea. In fact, I believe there is a ratio between the two. The abolition of horse transport in these islands accounts largely for the diminution of gastro-enteritis and purulent eyes. The World Health Organization must be thanked for that.

I can offer one quite effective diagnostic tip to those who have to survey wide areas in the outback of this country. There is no need to evert the upper eyelid in a vast survey. If the syndrome of trachoma is present, the cornea will be lacking in sensitivity. Line the cases up in rows of 50, and give each examiner or teacher, who, I understand, do most of this work in north-west areas, a pledget of cotton wool. As the patients file past, the cornea is touched centrally with a wisp of wool and those with an absent blink reflex or a sluggish response are "fallen out" and their lids are everted. In Polynesia these cases always proved to have granulations and pannus; presumably the pannus has a constricting effect on the nerve supply to the cornea by scar-tissue formation.

There is one more point of interest in dealing with a trachomatous eye, complicated by cataract. Remove the lens by the inferior route, as otherwise one gets a marked flare-up of the pannus, which is mostly confined to the upper limbus. The same applies to leprotic eyes with secondary cataract.

Yours, etc.,

PATRICK DALY.

Padbury House,
170 St. George's Terrace,
Perth, W.A.
July 14, 1960.

SURGERY AND THE GENERAL PRACTITIONER AND PROFESSIONAL UNITY.

SIR: Like many others, I have followed with great interest the discussion in your Journal which has followed that regrettable article in *The Australian Women's Weekly*. I am grateful to Dr. McDonald, Dr. Godfrey and Dr. Jackson on the one hand, and to Dr. Hoy on the other, for expressing my sentiments so admirably. Dr. Bothroyd's letter of July 2 astounds me. I have had 40 years of general practice, half of which was spent in the country. Like him, I have seen or heard of some work which left much to be desired; but I object emphatically to his conclusions and his proposed remedies. The latter are particularly undesirable. Over the course of many years, I have seen work done by specialists in surgery which was gravely lacking in judgement and in technique; yet to use such for the purpose of belittling surgery in Australia, of which we are justly proud, would be as silly as that displayed in Dr. Bothroyd's letter. As Dr. Hoy states, this is a country of great distances, and, except to those who are purely urban-minded or specialist-obsessed, competent general practitioners must be the backbone of the profession in Australia. Unlike Dr. Bothroyd, my twenty years in the country have left me with a profound admiration for my colleagues as men who were competent and possessed sound and shrewd judgement.

His suggested remedies deserve careful consideration, as they are the shadows of things which may yet come. This invitation to the Government to interfere yet further in professional practice is deplorable, and will be hailed with delight by the McKennas of the future. No Government has anything but the most superficial understanding of medical practice, which has been slowly evolved over many centuries, or the importance of the doctor-patient relationship. We have recently suffered the experience of our profession being made a political plaything by the present Government without reference to or seeking advice from the representatives of the profession. The supine way in which it has been accepted augurs badly for future resistance to further interference for party political reasons. Dr. Bothroyd allows that the benevolent Government may permit us to operate "under exceptional circumstances". Every country general practitioner can cite many such surgical incidents; may I quote a couple as illustration? Eight ectopics in the first 18 months of a certain practice, some of them tubal rupture and easily diagnosed, others tubal abortion requiring keen observation and judgement before diagnosis. A man with ruptured duodenal ulcer riding his bike 20 miles to the nearest centre of transport. Dr. Cameron and his advisers in the Health Department might graciously admit most of those as being exceptional circumstances; but it was well for the patients that the general practitioner concerned had already acquired some surgical ability.

Among the "approved surgeons" may be included "one who over the years has become recognized as having exceptional ability". I can think of many who would qualify; but how would they attain such recognition without having had the opportunity of practising and demonstrating such ability? It all represents confused thinking. The nationalized health scheme is a really bright idea, and will eventually be brought forward by either of the two parties either for party political or for ideological reasons. So we will, as in England, have general practitioners acting as relaying stations to an ever-increasing swarm of specialists. Then let us have a four-year course—six years is waste of time, money and energy—with a L.P.M. degree ("Licensed to Practise Medicine"). Rather rough on many people in country areas; but their voting strength is not sufficient to neutralize ideological urges, so why worry?

But what is going to happen when the next big move does come? We are told that the profession in England was sold out by the ineptitude of its national Council. While I am sure the members of our Federal Council are all worthy gentlemen, we must remember they are mainly specialists, and if there should be many among them with the *Women's Weekly*-Bothroyd outlook, then we will be sold out indeed beyond redemption. Let us beware.

Yours, etc.,

P. L. DANIEL, M.B.

Kensington,
New South Wales.
July 11, 1960.

INTERNATIONAL ASSOCIATION FOR DENTAL RESEARCH: AUSTRALIAN SECTION.

SIR: At a meeting held on Tuesday, July 5, 1960, an Australian Section of the International Association for Dental Research was formed. It is hoped that this will provide a means of stimulating interest in research in all branches of dental science and in the related phases of the sciences and will provide a common meeting ground where help may be offered and achievements discussed.

Membership of this section is secondary to membership in the parent association. Eligibility for membership of the parent body requires that a person should have displayed his interest in dental science and dental research by (*a*) research in process or conducted in the past, (*b*) scientific papers based upon original research presented before national or international meetings or (*c*) scientific papers based upon original research and published in scientific journals. New members may be elected only at general meetings.

Should any of your readers desire membership, the officers of the Australian Section would be pleased to arrange for their proposal to the parent body. I would be happy to furnish any information to any interested person.

Yours, etc.,

H. R. SULLIVAN,
Honorary Secretary.

Australian Section,
International Association for Dental Research,
The Dental Hospital of Sydney,
Chalmers Street,
Sydney.
July 15, 1960.

TOTAL BLINDNESS FROM TEMPORAL ARTERITIS.

SIR: Following the article by Hugh Ryan in your issue of June 18, 1960, may I be permitted to make two observations?

Firstly, the treatment at the Victorian Eye and Ear Hospital during recent months of at least five cases of biopsy-proven giant-cell arteritis associated with gross visual loss indicates that the such occurrence is not uncommon. (Two cases were also seen in the private practice of the writer and his partner, J. Paul Borger.)

Secondly, in spite of the usual treatment being instituted shortly after the vision of the first eye is lost, the other eye may rapidly become totally blind. This is illustrated by a female patient, aged 70 years, recently under my

care at the Victorian Eye and Ear Hospital. This woman was admitted on July 21, 1959, with a history of rapid failure of vision of one eye over the previous five days until there was then no perception of light in that eye; the other eye had visual acuity of 6/9. Steroids were administered from admission; the following day biopsy report of temporal artery confirmed the diagnosis of giant-cell arteritis. One day later the other eye began to lose vision, and anticoagulant therapy was instituted and steroids continued. But, unfortunately, in another three days both eyes were without perception of light, and have remained so. Optic atrophy developed in both eyes.

Yours, etc.,

KELVIN LIDGETT,
Honorary Ophthalmic Surgeon.

Victorian Eye and Ear Hospital,
Melbourne.
July 18, 1960.

ATTEMPTED SUICIDE, WITH SPECIAL REFERENCE TO BROMUREIDES AND SIMILAR PREPARATIONS.

SIR: There seems to be a certain lack of logic in the proposal, put forward again recently in articles in the July 2 edition of the Journal, that the open-chain ureides (carbromal, etc.) be obtainable only by doctor s prescription. This is suggested because a number of cases of bromide psychosis resulting from over-dosage with these drugs are occurring. However, in Queensland, where the sale of the ureides is thus restricted, bromism due to the unrestricted sale of potassium bromide mixtures is still common. My impression was that it was rather more common on a per-capita basis than in Sydney and Melbourne where the sale of the ureides is not controlled. It would seem most unwise to restrict the use of ureides if potassium bromide remains available as an alternative, as to be effective this latter drug required much higher blood bromide levels.

Further, when it is remembered that the number of cases of bromide psychosis reported is only a fraction of the number of cases of alcoholic psychosis occurring in the same period of time, and that the great majority of bromide psychoses are reversible whereas many of the alcoholic are not, the logic of the proposal becomes questionable. It is to be hoped that before such suggestions are implemented research will be carried out as to the number of people in the community relying on the use of open-chain ureides as a mild sedative, and as to what alternative methods they will adopt if this is withdrawn. Perhaps, because many of the people who protest against the use of this drug prefer to take alcohol for a possibly similar reason, they are able to detect the mole-hill of bromide psychosis without observing the mountain of alcoholic psychosis alongside.

Yours, etc.,

N. MCCONAGHY.

5 Collins Street,
Melbourne.
July 18, 1960.

SMALLPOX VACCINATION.

SIR: I have just read the letter from Dr. G. Beumer which appeared in your issue of June 25, 1960, concerning the site for vaccination against smallpox.

All Local Authorities in this State vaccinate on the arm (preferably the left arm) at the insertion of the deltoid muscle. This is regarded as the most suitable area, on account of its satisfactory lymph drainage and its low risk of exposure to trauma. There is ample authority to quote for the selection of this site (Commonwealth Serum Laboratories, 1956; Ministry of Health, 1948; Nelson, 1959; Parish, 1951; Rivers and Horsfall, 1959). The leg is not recommended, and I have seen some very severe reactions due to vaccinations on the thigh. I have had no experience of the sole of the foot as a site for inoculation in babies, but I should imagine that it would be subject to more trauma than the upper arm.

I hope that Dr. Beumer is convinced that the upper arm is recommended for very good reasons other than the reason that it is "handy".

Incidentally, I believe that Queensland is the only State which is attempting to implement the 1958 recommendation of the National Health and Medical Research Council that infants should be vaccinated against smallpox in the first year of life, and in this State we are now vaccinating children up to the age of five years because generalized reactions are uncommon.

The continued occurrence of smallpox in countries and islands to the north of Australia, and the almost completely unprotected state of the Australian population should smallpox be introduced, are two very strong reasons why the medical profession should advocate vaccination of infants.

Yours, etc.,

D. W. JOHNSON,
Deputy Director-General of Health and Medical Services.

Department of Public Health, Queensland,
Brisbane,
July 8, 1960.

References.

COMMONWEALTH SERUM LABORATORIES (1956), "Handbook of Instructions": 97.

MINISTRY OF HEALTH (1948), "Memorandum on Vaccination against Smallpox", H.M.S.O.

NELSON, W. E. (1959), "Textbook of Pediatrics", 7th Edition: 502.

PARISH, H. J. (1951), "Bacterial and Virus Diseases", 2nd Edition: 153.

RIVERS, T. M., and HORSFALL, F. L. (1959), "Viral and Rickettsial Infections of Man", 3rd Edition: 685.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE THE UNIVERSITY OF SYDNEY.

Week-End Conference at Newcastle (Medicine).

THE Post-Graduate Committee in Medicine in the University of Sydney, in conjunction with the Central Northern Medical Association, will hold a week-end conference in Room 35S, Technical College, Maitland Road, Islington, on Saturday and Sunday, August 13 and 14, 1960. The programme is as follows:

Saturday, August 13: 2 p.m., Registration; 2.15 p.m., "Acute Myocardial Infarction", Dr. W. A. Seldon; 2.45 p.m., "Management of Ischæmic Heart Disease", Dr. Douglas Stuckey; 3.30 p.m., "Electrocardiography—Practical Session", Dr. G. E. Bauer; 4.15 p.m., Discussion.

Sunday, August 14: 10 a.m., "The Position of Surgery in Mitral and Aortic Valve Disease", Dr. Douglas Stuckey; 10.30 a.m., "Recent Advances in Hypertension", Dr. G. E. Bauer; 11.15 a.m., "Management of Heart Failure", Dr. W. A. Seldon; 11.45 a.m., Discussion.

The combined fee for attendance is £3 3s., or £1 1s. per Section. Those wishing to attend are requested to notify Dr. R. V. Dan, Honorary Secretary, Central Northern Medical Association, 17 Bolton Street, Newcastle, as soon as possible. Telephone: Newcastle B 2244.

The Section on Surgery will be held on October 22 and 23, 1960.

THIRD AUSTRALASIAN CONFERENCE ON RADIOBIOLOGY.

THE third Australasian Conference on Radiobiology will be held at the School of Public Health and Tropical Medicine, Sydney, from Monday to Thursday, August 15 to 18, 1960, under the sponsorship of the Post-Graduate Medical Foundation, University of Sydney.

Registration forms and fee of two guineas ($5.00) will be accepted by the Convener, Dr. Peter Ilbery, Department of Preventive Medicine, University of Sydney, up to the date of the Conference. Registration may also be made in the Conference Room, The School of Public Health and Tropical Medicine, University of Sydney, from 9 a.m. to 9.30 a.m. prior to the official opening, or at any other time during the Conference. Early registration would be appreciated.

All lectures will be in the main Economics Lecture Theatre, R. C. Mills Building, Fisher Road, adjacent to the School.

The programme is as follows:

Monday, August 15: 9 a.m., registration. 9.30 a.m., official opening: foreword, Mr. V. M. Coppleson; welcome, Sir Edward

Ford; official opening, Emeritus Professor S. H. Roberts, C.M.G. 11 a.m. (chairman, Dr. G. M. Watson), "The Stepwise Development of the Radiation Injury at the Cellular Level; Role of Radiation Chemistry", Dr. Peter Alexander, Chester Beatty Research Institute, London; "Effects of Gamma Radiation on Ribo Nuclease", Professor S. Rubenfeld, Bellevue Hospital Medical Center, New York; "Chromosome Damage Produced by Radiations", Dr. J. H. Read, British Empire Cancer Campaign Radiation Biology Group, Dunedin. 2 p.m. (chairman, Dr. S. Fazekas de St. Groth), "Cytogenic Analysis of Cell Populations in Radiation Chimæras", Dr. C. E. Ford, Medical Research Council Radiobiological Research Unit, Harwell; "Retransplanted Hæmatopoietic Homografts Through Radiation Chimæras", Dr. C. E. Ford, Dr. P. L. T. Ilbery and Miss S. M. Winn, Department of Preventive Medicine, University of Sydney; "Further Experiments in Homograft Survival', Dr. M. Kent, Department of Surgery, University of Melbourne; "Preservation of the Radiation Protection Factor by Freezing", Dr. Phan The Tran, Department of Radiobiology, Atomic Energy Office, Saigon, and Dr. M. A. Bender, Oak Ridge National Laboratory, Tennessee. 4 p.m., "The Effect of Radiation on the Immune Response", Professor P. C. Koller, Chester Beatty Research Institute, London.

Tuesday, August 16: 9.30 a.m. (chairman, Professor H. K. Ward), "Components of Radiation Carcinogenesis", Dr. Jacon Furth and Dr. K. Yokoro, Roswell Park Memorial Institute, Buffalo; 11 a.m., "The Application of the Two-Stage Mechanism of Carcinogenesis to Leukæmogenesis with Low Doses of X Rays as the Initiating Factor", Professor I. Berenblum, Weizman Institute, Rehovoth, Israel; "Radiation in the Ætiology of Sporadic Human Leukæmia", Dr. F. W. Gunz, Christchurch Hospital, New Zealand; 12 noon, "Radiation-Induced Ageing in Mice", Dr. H. J. Curtis, Brookhaven National Laboratory, Long Island; 2 p.m. (chairman, Professor J. L. Still), "Chemical Protection Against Radiation in Vivo and in Vitro", Dr. Peter Alexander, Chester Beatty Research Institute, London; "Comparative Evaluation of Radioprotective Efficacy of Cysteamine against 500r Whole Body Irradiation with Different Biological Reference Systems", Dr. P. De, Chittaranjan Cancer Research Hospital, Calcutta; 3.30 p.m., "Chlorpromazine and Radiation Protection in Vivo", Dr. H. Van den Brenk and Mrs. D. Jamieson, The Cancer Institute, Melbourne; "The Radiation Resistance of Bacterial Spores", Dr. W. G. Murrell and Dr. W. J. Scott, Commonweath Scientific and Industrial Research Organization, Division of Food Preservation, Homebush; "Some Measurement of Environmental Activity in N.S.W.", Dr. E. T. Pallister, Dr. D. J. Carswell and Dr. J. H. Green, University of New South Wales, Kensington; "Results of ^{90}Sr Determinations on Samples from Lucas Heights and Richmond", Dr. L. E. Smythe and Mr. P. S. Davis, Australian Atomic Energy Commission Research Establishment, Lucas Heights; "The Determination of ^{90}Sr in Biological Materials by an Ion-Exchange Method", Mr. P. S. Davis, Australian Atomic Energy Commission Research Establishment, Lucas Heights; "Sr and ^{90}Sr in Bone Using More Rapid Methods", Miss P. M. Horsford, Department of Preventive Medicine, University of Sydney.

Wednesday, August 17: 9.30 a.m. (chairman, Professor Th. Dobzhansky), "Delayed Effects of Radiation on Seeds", Dr. H. J. Curtis, Brookhaven National Laboratory, Long Island: 11 a.m., "Radiation-Induced Quantitative Variation in Subterranean Clover', Dr. R. D. Brock and Dr. B. D. H. Latter, Commonwealth Scientific and Industrial Research Organization, Division of Plant Industry, Canberra; "The Modification of Genetic Response to X-Irradiation in Drosophila Melanogaster", Professor A. H. Clark, Zoology Department, University of Tasmania; "The Influence of Ultra-Violet Irradiation on General Transduction in Pseudomonas Aeruginosa", Dr. B. W. Holloway and Miss M. Monk, Department of Bacteriology, University of Melbourne; "Effects of X-Irradiation on the Endogenous and Auxin-Induced Growth of Pea Stem Sections", Professor A. W. Galston and Dr. J. W. King, Yale University, Connecticut.

The afternoon is free. A visit to the Australian Atomic Energy Commission Research Establishment at Lucas Heights can be arranged for this afternoon.

Thursday, August 18: 9.30 a.m. (chairman, Dr. H. J. Ham), "The Use of Ionizing Radiation in the Study of Immunity to Parasitic Nematodes", Dr. W. Mulligan and Dr. D. F. Stewart, Division of Animal Health, McMaster Laboratory, Sydney; "Cytological Assessment of Cancer of the Cervix following Treatment by Irradiation", Dr. K. A. McGarrity and Dr. J. Garven, St. Vincent's Hospital, Sydney; 11 a.m. (chairman, Professor B. J. F. Ralph), "An Electron Microscopic Study of a Transmissible Radiation-Induced Leukæmia", Dr. H. Hoffman and Miss N. Darveniza, Commonwealth Scientific and Industrial Research Organization, Animal Genetics Section, University of Sydney; "The Mechanism of Photosensitivity", Dr. V. J. McGovern, Department of Pathology, Royal Prince Alfred Hospital, Sydney; "Beta Radiation and Protoporphyrin Biosynthesis', Mr. R. Tirrell, School of Biological Sciences, University of New South Wales; "Radiation Synthesis of Amino Acids from Gas Mixtures", Dr. S. Dilli and Dr. J. H. Green, Department of Nuclear Chemistry, University of New South Wales; "Oxidative Effects of Ionizing Radiation and of Ozone on the Cytochromes of Torulopsis Utilis", Mr. E. E. Malone, University of New South Wales; "The Adaptive Response of a Yeast to Hydrogen Peroxide", Mr. B. P. McBrien, School of Biological Sciences, University of New South Wales. 2 p.m. (chairman, Professor R. H. Thorp), "Comparison of the Histological Effects of Radiation and Radiomimetic Chemicals", Professor P. C. Koller, Chester Beatty Research Institute, London; "Comparative Biochemistry of Radiomimetic Chemicals and Radiation", Dr. Peter Alexander, Chester Beatty Research Institute, London; "Comparison of the Effects of Radiomimetics and Radiation on Hæmatopoiesis", Dr. D. A. G. Galton, Chester Beatty Research Institute, London.

ROYAL PRINCE ALFRED HOSPITAL: EAR, NOSE AND THROAT DEPARTMENT.

Seminar Programme, 1960.

THE staff of the ear, nose and throat department of the Royal Prince Alfred Hospital will conduct a seminar on the second Saturday of every month at 8 a.m. in the Scot Skirving Lecture Theatre. The main speaker will not exceed forty minutes, and there will be a discussion at the conclusion of his remarks. All medical practitioners and clinical students are invited to attend.

At the next seminar, to be held on August 13, 1960, Dr. H. D. Raffan and Dr. H. Kronenberg will speak on "Bleeding Disorders in Ear, Nose and Throat Surgery".

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

General Practitioners' Refresher Course in Medicine and Surgery.

THE Melbourne Medical Post-Graduate Committee announces that a general practitioners' refresher course in medicine and surgery will be held in September, 1960, at St. Vincent's Hospital. The programme is as follows:

Monday, September 5: 9 a.m., "Diarrhœa and Malabsorption Syndrome"; 11 a.m., orthopædic case presentation and discussion, Mr. B. Dooley; 2 p.m., "Anæsthesia in General Practice", Dr. R. R. Clark; 4 p.m., "Burns', Mr. R. K. Newing.

Tuesday, September 6: 9 a.m., "Peptic Ulceration", Mr. J. L. Connell; 11 a.m., symposium, "Hypertension and Coronary Artery Disease", Professor J. Hayden, Dr. J. Cahill, Dr. L. Murphy; 2 p.m., "Common Ophthalmological Conditions", Mr. Hugh Ryan; 4 p.m., "Renal Disease and Diuretics", Dr. J. F. Niall.

Wednesday, September 7: 9 a.m.: "Dermatology", Dr. J. Brenan; 11 a.m., "Common Fractures", Mr. W. R. Gayton; 1 p.m., clinico-pathological meeting; 2 p.m., surgical quiz session, Mr. A. R. Kelly, Mr. K. Rush, Mr. R. H. Hadley, Mr. G. Brosnan; 4 p.m., "Recent Advances in Therapeutics", Dr. R. M. Biggins.

Thursday, September 8: 9 a.m., "Cardiac Emergencies", Dr. M. V. Clarke; 11 a.m., "Gynæcological Emergencies in Surgery", Mr. F. J. Hayden; 1 p.m., films and discussion, "Cardiac Arrest and Artificial Respiration", Dr. R. R. Clark; 2 p.m., "Diabetes", Dr. W. Hamilton Smith; 4 p.m., "Ano-Rectal Conditions", Mr. J. R. McCoy.

Friday, September 9: 10 a.m., visit to Geriatric Unit, Mount Royal, Dr. R. F. Butterworth; 2 p.m., "The Acute Abdomen", Mr. Peter Ryan; 4 p.m., "Problems of Arthritis", Dr. J. Webb.

Saturday, September 10: 9.30 a.m., neurological demonstration and discussion, Dr. J. J. Billings.

The fee for this course is £9 9s. Applications for enrolment should be sent to the Melbourne Medical Post-Graduate Committee, 394 Albert Street, East Melbourne, by August 22.

A Correction: Lecture by Mr. Norman Tanner.

The Melbourne Medical Post-Graduate Committee draws attention to Mr. Norman Tanner's lecture on "Hiatus Hernia". This will now be delivered on Friday, August 12, at 8.15 p.m. in the Medical Society Hall, East Melbourne. This corrects the previous announcement which gave the date as Thursday, August 11.

Notes and News.

World Congress of Psychiatry.

The Third World Congress of Psychiatry is being held from June 4 to 10, 1961, at Montreal, Canada, at the invitation of McGill University and under the auspices of the Canadian Psychiatric Association. Meeting on the American continent for the first time, the Congress is expected to attract some 3000 delegates from 62 nations. Representatives will come from psychiatry and such allied fields as general medical practice, psychology, biochemistry, nursing, sociology, anthropology, social work and pharmacology. Copies of the second announcement, which carry information regarding programme and registration, may be obtained by writing the General Secretary, III World Congress of Psychiatry, 1025 Pine Avenue West, Montreal 2, P.Q., Canada.

Seminar on Rehabilitation at "Mt. Wilga", Hornsby, N.S.W.

The Commonwealth Rehabilitation Service (Department of Social Services) announces that a seminar on "Medicine, Surgery, General Practice and Rehabilitation in the Commonwealth Rehabilitation Service" will be held on Saturday, September 24, 1960, from 10.45 a.m. to 4 p.m., at the Commonwealth Rehabilitation Centre, "Mt. Wilga", Manor Road, Hornsby. The guest chairman will be Dr. K. B. Noad. Members of the medical profession are invited to attend this seminar. There is no fee for attendance. Lunch and afternoon tea will be provided by courtesy of the Commonwealth Department of Social Services. To assist with catering, those who propose or intend to be present, are asked to notify the Secretary to the Senior Medical Officer (Social Services), Sydney, telephone BO 234, extension 387. The meeting on this occasion is necessarily restricted to medical practitioners, for reasons of space, etc.

Road directions are as follows: Proceed on the Pacific Highway. Pass through the Hornsby shopping centre, and continue on for about one mile to a five-ways (Galston Gorge, Berowra Waters, etc.) turn-off. Turn hard left into Carrington Street, and proceed until its termination in a T intersection. Turn left into Manor Road, and the main gates of the Centre will come into view within about 30 yards. Visitors will be met on arrival. The travelling time from Sydney Harbour Bridge to Mt. Wilga is approximately 45 minutes.

Russian Poliomyelitis Drug, Karantonin.

The Commonwealth Minister for Health, Dr. D. A. Cameron, has warned poliomyelitis sufferers against basing exaggerated hopes on recent cabled reports concerning the new Russian drug, karantonin. This drug was referred to in cabled reports as being a cure for paralysis. Dr. Cameron said that inquiries in Russia had identified the drug as physostigmine, otherwise known as eserine. This drug was readily available in Australia. Its action was to stimulate the activity of muscles, and to this extent it could be a useful adjunct to physiotherapy in an attempt to save temporarily inactive muscles from permanent paralysis. The Russians had made no claim for the drug in the treatment of poliomyelitis except in the first stages of the disease. Disappointing though it might be, no victim of poliomyelitic paralysis of long standing could expect any drug to effect a real or lasting improvement.

New Monograph Series Published by American Heart Association.

A new monograph series of interest to physicians, investigators and students in the cardio-vascular field has been inaugurated by the American Heart Association. First publication in the series, a "Symposium on Congestive Heart Failure", brings together articles published originally in the January, February and March issues of *Circulation*, monthly journal of the American Heart Association. These were edited by Herman L. Blumgart, M.D., editor-in-chief of *Circulation*. Included are review articles by leading cardiologists on "Starling and the Concept of Heart Failure", "Hemodynamic Aspects of Congestive Heart Failure", "Metabolism of the Heart in Failure", "Kidney in Congestive Heart Failure", "Unusual Causes of Heart Failure", "Clinical Management of Congestive Heart Failure", "Correction of Hyponatremia in Congestive Heart Failure", "Clinical Consideration of Cor Pulmonale", "Pediatric Aspects of Congestive Heart Failure", "Congestive Phenomena Occurring in Pregnant Women with Heart Disease", and "Rehabilitation in Congestive Heart Failure". Copies may be obtained at $2.00 from the Distribution Department, American Heart Association, 44 East 23rd Street, New York 10, N.Y., U.S.A.

Worcester Foundation for Experimental Biology: Training Programme in the Physiology of Reproduction.

In recognition of the world-wide need for scientific training in reproductive physiology, the Worcester Foundation for Experimental Biology plans to initiate on January 1, 1961, a post-graduate programme in this field under a grant from the Population Council. Fellowships for the programme will be awarded to candidates possessing the Ph.D. or M.D. degrees, or their equivalents. These fellowships will carry a stipend of $5500 *per annum*, and will be for a twelve months' period. An allotment will also be made for round-trip travel to Shrewsbury, Massachusetts. Application forms may be secured from the Research Director of the Worcester Foundation for Experimental Biology, and should be returned at an early date. They will be examined by a selection committee of experts, and the fellowship awards for the first year will be announced late in 1960. Applicants for participation in the programme in 1962 and later years may communicate with the Director at any time, but their applications will not be acted upon in 1960.

The programme will consist of a course of lectures and laboratory work. During the latter part of the year each Fellow will have the opportunity to participate in a research project pertinent to his interests and within the capacity of the programme.

The lecture series will be given by the Programme Director, various members of the staff of the Worcester Foundation, and guest experts. The lectures and accompanying laboratory work will cover various phases of reproductive processes, particularly in mammals. Subjects to be treated will involve a review of reproductive processes in the male, including consideration of spermatogenesis, hormonogenesis, the control of testis function, and the functional endocrinology of testis hormones. Extensive attention will be given to oogenesis, ovulation, and fertilization in the female, factors affecting the entire course of pregnancy and embryonic development, as well as the postnatal physiology of the female. Additional topics will include the role of extra-reproductive tract organs in reproductive processes, genetic and nutritive factors in reproduction, and the control of fertility and sterility.

Laboratory exercises will include the study of characteristic reproductive phenomena in various species, analytical procedures employed in determining the chemistry of reproductive organs, the biochemistry of spermatozoa and ova, and hormone analyses pertinent to gonad function, to sex cycles, to gestation and to lactation.

A Journal of Child Psychology and Psychiatry.

Pergamon Press has undertaken the publication of a new quarterly journal, *The Journal of Child Psychology and Psychiatry*, which is to be the official organ of the Association of Child Psychology and Psychiatry. In planning it the aim was to bring together original papers concerned with the child from such diverse disciplines as psychiatry, psychology, pædiatrics, psychoanalysis, social case work and sociology. Those responsible for the journal consider it important to balance and complement those approaches that study the child as an individual organism with those which view him as a developing social being, whose feelings and interests are aroused, and whose attitudes are shaped, by his constant interaction with the family and society. The value of comparative studies in cultural anthropology and animal behaviour is also recognized. The annual subscription rate to this new journal is £3 3s. (inclusive of membership) to members of the Association of Child Psychology and Psychiatry, £5 5s. to private individuals and £7 per volume to libraries and institutions. Inquiries regarding subscriptions may be directed to the Pergamon Press, 4 and 5 Fitzroy Square, London, W.1.

Notice.

BRITISH MEDICAL ASSOCIATION: VICTORIAN BRANCH.

Section of Industrial Medicine.

A MEETING of the Section of Industrial Medicine of the Victorian Branch of the British Medical Association will be held in conjunction with the Victorian Branch of the Australasian Association of Psychiatrists on Monday, August 15, 1960, in the Theatrette on the ground floor of I.C.I. House, 1 Nicholson Street, Melbourne, at 8 p.m. The subject for discussion is "The Early Recognition and Management of Alcoholism". The speakers will be Dr. J. H. Hurt, Dr. J. R. Moon and Mr. E. W. Corless, President of the Alcoholism Foundation of Victoria. All members of the Branch are invited to attend.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments and changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 34, of May 16, 1960.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The following Flight Lieutenants (Students) are appointed to a short-service commission on probation for a period of twelve months and with seniority in that rank as from 20th December, 1958:—B. Walters (037263), 31st December, 1959; P. B. Sims (0313287), A. V. L. Hill (036613), 10th January, 1960.

The resignation of the following Flight Lieutenants is accepted:—G. A. Tomkins (018879), 25th March, 1960; K. W. Prichard (055804), 31st March, 1960.

Active Citizen Air Force.

Medical Branch.

No. 24 (City of Adelaide) (Auxiliary) Squadron.—Flight Lieutenant D. B. McLeay (042513) is promoted to the temporary rank of Squadron Leader, 14th March, 1960.

No. 25 (City of Perth) Squadron.—Flight Lieutenant A. S. Luketina (040501) is transferred from the Reserve, 6th February, 1960.

Air Force Reserve.

Medical Branch.

John Dixon Lodge (268125) is appointed to a commission, 7th March, 1960, with the rank of Flight Lieutenant.

Flight Lieutenant (temporary Squadron Leader) N. V. Youngman (277630) is promoted to the temporary rank of Wing Commander, 14th March, 1960.

The following Flight Lieutenants are promoted to the temporary rank of Squadron Leader, 14th March, 1960:—J. S. Rodgers (267950), D. O. Tonkin (257967), J. D. Lodge (268125).

The appointment of Flight Lieutenant (temporary Squadron Leader) J. R. Radcliff (268024) is terminated 23rd March, 1960.

The entry in the notification regarding the termination of appointment of Flight Lieutenant (temporary Squadron Leader) N. V. Youngman (277630) as approved in Executive Council Minute No. 13 of 1959 appearing in Gazette No. 31, dated 21st May, 1959, is withdrawn.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JULY 2, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1	5(5)	..	..	..	..	..	..	6
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	7	..	7
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	21(19)	..	..	..	1	1	1	24
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	..	2(2)	..	1(1)	3(1)	..	4	..	10
Encephalitis	..	..	..	1	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	1	..	..	..	..	1	..	..	2
Infective Hepatitis	52(12)	19(11)	8(3)	19(8)	3(1)	..	1	1	103
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	1	..	1
Leptospirosis	..	..	2(1)	..	..	..	..	..	2
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	..	..	..	..	..	..	..	..
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	..	1(1)	..	..	..	..	..	..	1
Rubella	..	9(7)	..	..	..	..	1	..	10
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	17(7)	13(13)	5(3)	8(8)	1(1)	..	..	1	45
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	..	..	..	..	..	1
Trachoma	..	..	..	..	1(1)	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	17(9)	20(14)	14(7)	6(2)	11(7)	1	..	..	69
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales, in accordance with the provisions of the *Medical Practitioners Act*, 1938-1958.

Registered medical practitioners who are required to comply with the requirements of Section 17 (3) and are registered under Section 17 (1) (a) of the Act, qualifications being M.B., B.S., 1960 (Univ. Sydney) unless otherwise stated: Balzer, Noel Lancelot Edward; Burrow, Kerry Reginald; Chang, Peter Nang-Sang; Cumming, John; Dissevelt, Gerardus Johannes; Donnellan, Peter Michael; Facchini, Frederico John; Holcombe, Yvonne Margaret; Johnson, Adrian Paul; Khoo, Boo Yee; Lee, Thomas King Hing; Lloyd Bruce Logan; Marshall, John William; Mooy, Myles John, Nathaniel, Rajah Lionel; Nihill, Michael Robert; Redwin, Ronald James; Roncevich, Allan Leonard; Rutherford, Robert Bruce; Selby Brown, Colin; Ward, Christopher John Joseph; Ward, John Barrington; Whitton, James; Wilson, Robert Bruce; Xavier, Magimadass; Yap, Robert Tung Soh; Yip, Edwin Pah Wah.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (a) of the Act: Backhouse, Thomas Clive, M.B., Ch.B., 1917 (Univ. Melbourne); Cherny, Jack Casper, M.B., B.S., 1957 (Univ. Melbourne); Clarke-Jones, Robert David, M.B., B.S., 1956 (Univ. Melbourne); Eldred, Bernice Beatrice, M.B., B.S., 1950 (Univ. Queensland); Grant, John Mackinnon, M.B., B.S., 1948 (Univ. Melbourne); Macleod, Roy Maxwell, M.B., B.S., 1952 (Univ. Queensland); Stewart, Gordon John, M.B., B.S., 1951 (Univ. Melbourne); Wardlaw, Henry John, M.B., B.S., 1956 (Univ. Melbourne).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (b) of the Act: Bamford, Thomas Murray, M.B., B.Ch., 1950 (Univ. Dublin); Chatz, Theodore Lionel, M.B., B.Ch., (Univ. Witwatersrand); Henderson, George Sinclair, M.B., Ch.B., 1954 (Univ. Glasgow), D.P.H. (Glasgow), 1958; Keskevick, Alexis, L., L.M., R.C.P. (Ireland), 1956, L., L.M., R.C.S. (Ireland), 1956; Lyons, Edward David, M.B., B.Ch., 1950 (Univ. Witwatersrand), D.T.M. & H. (Sydney), 1959; Parker, Desmond Arthur Aloysius, M.B., Ch.B., 1945 (Univ. Glasgow); Thomas, James Livingstone, M.R.C.S. (England), L.R.C.P. (London), 1945; Waters, Maurice Hubert, M.B., B.Ch., 1939 (Univ. Dublin).

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Branch of the British Medical Association:

O'Neill, Charles Main, M.B., B.S., 1956 (Univ. London), Princes Highway, Unanderra.

Haskins, Jan Margaret, M.B., B.S., 1959 (Univ. Sydney), 2 Glendale Road, Turramurra.

Peak, Howard John, M.B., B.S., 1959 (Univ. Sydney), 90 Ryde Road, Pymble.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Colless, Helen Wynn, M.B., B.S., 1957 (Univ. Sydney); Scalzo, Giglio, M.D., 1946 (Univ. Bari, Italy), licensed under Regional Registration. Taralga Region; Protopopoff, Nicholas Paul, M.D., 1917 (Univ. Odessa) licensed under Section 17B, *Medical Practitioners Act*, 1938-1958; Lam, Thomas Sit-Tin, M.B., B.S., 1959 (Univ. Sydney); Sinnett, Peter Frank, M.B., B.S., 1960 (Univ. Sydney); Lyons, Edward David, M.B., B.Ch., 1950 (Univ. Witwatersrand); Sachs, Martin, M.B., B.S., 1960 (Univ. Sydney).

Deaths.

THE following deaths have been announced:

CAMERON.—Robert Miles Fletcher Cameron, on June 12, 1960, at Melbourne.

MEYER.—Moritz Meyer, on July 22, 1960, at Melbourne.

ROSENTHAL.—David Braham Rosenthal, on July 25, 1960, at Drouin, Victoria.

ANDREW.—Marshall Andrew, on July 26, 1960, in Wales, Great Britain.

Diary for the Month.

AUGUST 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
AUGUST 11.—New South Wales Branch, B.M.A.: Public Relations Committee.
AUGUST 12.—Tasmanian Branch, B.M.A.: Branch Council.
AUGUST 12.—Queensland Branch, B.M.A.: Council Meeting.
AUGUST 15.—Victorian Branch, B.M.A.: Finance Sub-Committee Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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